NATURAL RESOURCES DEFENSE COUNCIL

BY HAND DELIVERY

May 31, 2002

Docket ID No. OEI-10014
U.S. EPA
Northeast Mall
Room B607
401 M. Street SW
Washington, D.C. 20460

Re: Comments regarding EPA Draft Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information

To the Docket:

Enclosed for filing please find the comments of the Natural Resources Defense Council with respect to the above-referenced guidelines, which were noticed in the Federal Register on April 30, 2002. (67 Fed. Reg. 21234). The comments include three attachments.

Thank you.

Sincerely,

Rena I. Steinzor

Enclosure

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Comments
of the
Natural Resources Defense Council
regarding
EPA Draft Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency
May 31, 2002

The Natural Resources Defense Council submits these comments on *EPA's Draft Data Quality Act Guidelines* [*EPA Draft Guidelines*], noticed in the Federal Register on April 30, 2002 (67 Fed. Reg. 21234) and available at www.epa.gov/oei/qualityguidelines. NRDC is a national, non-profit organization of scientists, lawyers, economists, and other environmental specialists dedicated to protecting public health and the environment. Founded in 1970, NRDC has more than 500,000 members nationwide, and four national offices in New York, Washington, Los Angeles, and San Francisco.

The Data Quality Act ("Act"), enacted without debate as an obscure amendment to a massive budget bill, provides no guidance on how to implement its vague directives. Of course, no one can possibly be opposed to the Act's goal of improving data quality within the government. As John Graham, the director of the Office of Information and Regulatory Affairs has stated, however, the real question is "at what cost?" Vague and open-ended calls for "better quality" data must not be allowed to trump the purposes of detailed and carefully crafted statutes.

Accordingly, in developing guidelines to respond to the Act, EPA must seek guidance in requirements and public policy purposes set forth in the more detailed, pre-existing provisions of EPA's authorizing statutes and federal administrative law. EPA's authorizing statutes require the Agency to act on a timely basis to address risks to health and the environment and to do so using information that is appropriate to support its

health and environmental protection obligations. These laws further establish a presumption that EPA will carefully consider the added risks to the public that may flow from delaying action in order to acquire more or "better" data. Numerous judicial rulings affirm that EPA should err in the direction of protecting the public when carrying out its non-discretionary duties.

Meeting the challenge of improving data quality without undermining EPA's policy and legal obligations is more than merely desirable, it is essential because the goal of improving data quality is only one of several goals that agencies like EPA must achieve. Taking timely and effective action in response to threats to public health is at the core of EPA's mission – transcending other, less important mandates – and this core mission was not affected by passage of the Data Quality Act. Nothing in the language of the Data Quality Act can be read as an explicit or implied repeal or amendment of any of the substantive, procedural, or deadline provisions in the environmental statutes that EPA is charged with implementing. All of these principles should govern EPA in drafting guidelines to implement the Data Quality Act.

EPA has already taken many steps to improve the quality of the data it uses to make decisions and, had the Data Quality Act never been enacted, would undoubtedly have continued on that course. The challenge now is for the Agency to continue that work, listening to complaints about incorrect data and disposing of them expeditiously without committing inordinate resources or time to the effort. The Agency should also prepare to fight the inevitable efforts to drag such disputes into court.

If EPA implements the Act with courage and wisdom, as it has begun to do, data quality requirements will take their appropriate place beside other, equally compelling procedural values and requirements, such as transparency in government, public participation at all stages of the decision-making process, and timely decision making on threats to public health and the environment. If, on the other hand, EPA heeds the strident threats and grandiose claims regarding the Act's implications now being asserted

by some industry advocates, and engages in self-censorship in a futile effort to placate those who hold such extreme views, the Data Quality Act will become a potent source of gridlock, making the Agency's achievement of its many challenging statutory mandates that much more difficult.

While our principal concern in submitting these comments is the impact of an extremist data quality crusade on public health and the environment, we also note that government actions desired by industry would also be impeded by attempts to apply the Act in a sweeping form. For the Data Quality Act is a double-edged sword, as we will explain in these comments, and those who seize it too tightly may well suffer more costs than they reap benefits. The Act is double-edged because much of the information submitted to EPA in support of specific decisions is generated by industry with the intent that the Agency adopt the information as its own to support the desired outcome.

Four specific examples of this phenomenon – the Agency's decision to downgrade the toxicity profile of vinyl chloride, its pending decision to issue a toxicological profile for butadiene, its use of the Calendex model to set pesticide tolerance limits, and its consideration of undisclosed financial impact data in developing effluent guidelines for the pulp and paper industry – are supported by fatally flawed and, in some instances, secret data supplied by industry. In the Brave New World of the Data Quality Act that is proposed by some industry advocates, none of these outcomes is supportable, signaling to industry proponents of such decisions the truth of the old adage "Be careful what you wish for."

If the Data Quality Act were taken to the extremes urged by some industry representatives, protective rulemaking may suffer a full-body blow, but many other industry-sponsored initiatives will also fail. In the end, overzealous implementation will signal the death knell of this hastily crafted law, as the agencies, their constituencies, and the courts recoil at the nightmare that is created.

The following comments make five points with respect to the *EPA Draft Guidelines*:

1. ***EPA has correctly resolved the two most important issues presented by the Act, deciding first that it will use existing procedures to evaluate the quality of data, especially in the context of rulemaking, and, second, that it will not acquiesce in efforts to obtain judicial review of its decision-making, an outcome that is not contemplated by the Act.*** The Agency is a pioneer in establishing effective mechanisms for correcting the data it uses on a daily basis and should be afforded significant deference as the Office of Management and Budget (OMB) oversees the Act's implementation. If EPA or OMB allow the Data Quality Act to be used to frustrate rulemaking, EPA will not only fail to fulfill its core mission, as defined by the numerous statutory mandates that Congress has developed over three decades, but both agencies will preside over delay that costs people their lives. As just one concrete example, 150,000 people have died prematurely in the five years since EPA first attempted to strengthen the regulation of particulate matter under the Clean Air Act. If the Data Quality Act becomes a vehicle for exacerbating such delays, many thousands more will also die, elevating the costs of the Act to monstrous proportions.

2. ***Because EPA has statutory mandates that transcend and are more specific than the Data Quality Act, it has an affirmative obligation to safeguard its ability to meet those mandates.*** Accordingly, EPA should strengthen its draft guidelines by adopting such modest changes as (a) establishing deadlines for requests to correct data and petitions to reconsider such requests; (b) withholding any designation of information as "influential" until either a data correction request is made or a final

agency action is taken; (c) adopting a procedure for allowing the public to comment on requests to correct information regarded as influential before it makes final decisions to revise the data; (d) clarifying that its intent to reject "frivolous" requests includes requests filed after the Agency has rejected other requests to correct the same or similar information; (e) expanding the information that must be provided by any person or organization that files a request to correct data; and (f) clearly stating that nothing in the Data Quality Act or EPA's guidelines shall be construed to amend or repeal any other statutory obligation of EPA, including deadlines to complete reports, issue rules, or take other actions. EPA is rightfully concerned about the implications of the Act as a massive "unfunded mandate" on state and local governments if it is not implemented wisely. These six modest changes will also assist its efforts to maintain an effective partnership with those entities.

3. ***The Toxic Release Inventory, Safe Drinking Water Information System, and similar data bases fall outside the scope of the Act because EPA is merely serving as a "conduit" for information generated by third parties.***

4. ***EPA already has sufficient mechanisms for ensuring that especially influential data is subject to peer review.*** In other contexts, NRDC has advocated strengthening the objectivity and transparency of peer review, and we believe the Agency has already begun to make these crucial changes. Those efforts should remain a priority, and EPA should reject demands that it drastically expand the scope of peer review, as advocated by some industry commentators.

5. ***EPA is correct in declining to apply the Safe Drinking Water Act's data quality provisions to the task of ensuring data quality in other contexts because, as a legal matter, those provisions apply only to decisions made***

under one specific section of that Act. OMB went far beyond its legal authority in insisting that every agency or department "adapt or adopt" those standards but, as an exercise of its sole discretion, EPA's resolution of this issue is appropriate. This point is especially crucial because risk assessment is an increasingly important methodology for Agency decision-making and misinterpretation of the Safe Drinking Water Act's provisions could lead to the erroneous view that all components of risk assessment are "factual" and therefore subject to the Act. NRDC strongly recommends that in its final *Guidelines*, EPA explain further why risk assessment is a judgmental tool that informs decisions based on science, fact, policy, economics, and – in most of its important statutes – the application of the precautionary principle, so that this confusion about the division between science, fact, law, and policy does not persist.

These comments consider the above issues in the following order: (1) why NRDC supports the *EPA Draft Guidelines*; (2) six modest changes that will help EPA conform its implementation of the Data Quality Act with its core statutory mission; (3) treatment of the Toxic Release Inventory and similar information; and (4) the application of the Safe Drinking Water Act's data quality provisions to peer review and to decisions that blend science, fact, law, and policy.

The Draft Guidelines: The Right Calls

EPA's Track Record and the Importance of OMB Deference

Long before the Data Quality Act became effective, EPA initiated unprecedented efforts to improve data quality, and it deserves considerable deference in the context of OMB's ongoing efforts to oversee efforts throughout the government to implement the Act. As explained by Elaine Stanley during the National Academy of Sciences workshop on the Data Quality Act, EPA is a pioneer among federal agencies and departments both in making information about public health and the environment

available to the public and in allowing the public to submit requests for correction of such data. National Academies of Science Workshop # 1, "Ensuring the Quality of Data Disseminated by the Federal Government," Science, Technology and Law Program, March 21, 2002 (Statement of Elaine G. Stanley, Transcript at 145-55) [hereinafter "NAS Workshop #1 Transcript"].

For example, EPA initiated a process allowing the public to submit data correction requests online. In the last 18 months, the Agency has received some 1000 notifications and submissions under this procedure. However, it has deemed only 300 to be valid in the sense that the request actually reported an error and gave EPA enough information to evaluate the request. Of those 300, about 120 resulted in the data being corrected, or approximately ten percent of all the requests that have been received. NAS Workshop #1 Transcript at 151.

OMB should support EPA's commendable efforts to make data correction widely and easily available to the public, as opposed to rendering it an inside-the-Beltway process understood and exploited only by well-financed interest groups. The simple fact that EPA engages in activities that upset powerful industries should not make it a poster child for continual scrutiny and interference with respect to its implementation of the Data Quality Act, as has been threatened by the Center for Regulatory Effectiveness ("CRE"), a right-wing think tank spearheaded by Jim Tozzi, a self-proclaimed architect of the Act.

CRE has already submitted a petition that includes a veiled threat to drag EPA to court if the Agency does not reverse a decision that it will wait for recommendations from the National Academies of Science regarding the ethics of human testing before considering such test results under the Federal Insecticide, Fungicide, and Rodenticide Act. NRDC full supports EPA's decision in this matter, not only for ethical and legal reasons but because the data in the underlying studies is fatally flawed.

The data from these human tests are flawed because the studies involved feeding

pesticides to a small group of adults, generally only males. Not only are the samples too small to produce statistically valid results, the reaction of these adult subjects to the doses they received is not applicable to the doses that may be ingested by children, who are the primary focus of the statutory requirements EPA must implement. Moreover, these industry-sponsored studies are not published or peer reviewed, and fail on several other counts to meet thresholds of scientific credibility.

The Administration will do great damage to its duty to faithfully execute the laws and to the credibility of the Data Quality Act as an expression of public policy if it supports or encourages the activities of Mr. Tozzi and his colleagues, activities that distort the Act and would render it nothing more than a tool to obstruct timely government decision-making.

Use of Existing Procedures and Safeguards

EPA is not only correct, but legally obligated, to take the position that it will not establish a separate track for review of the quality of data considered in a rulemaking, or any other process that is already subject to adequate safeguards to ensure data quality. As the Agency states in *Draft EPA Guideline* 5.4: "A separate process would be duplicative, burdensome, and disruptive to the orderly conduct of the action."

The reason why EPA is legally obligated to take this approach is that to do otherwise – that is, to set up an independent mechanism for the submission, consideration, and reconsideration of data quality correction requests – would inevitably cause it to breach more detailed statutory mandates it has already been assigned by Congress. As we noted at the outset, the Agency is subject to numerous important mandates set forth with specificity in several major statutes that Congress has reauthorized repeatedly over the last two decades. As just one example, the Safe Drinking Water Act's provisions on data quality, which OMB has incorrectly embraced as applicable to the entire government in the context of Data Quality Act implementation, were enacted as one part of major amendments to the law in 1996. Those amendments

also imposed new rulemaking mandates on EPA. The Agency is already way behind in implementing those requirements, as it is with respect to several other rulemaking mandates in other core statutes.

To argue that EPA is obligated to establish a separate process for ensuring data quality, one that permits interlocutory appeals that could bring mandated rulemaking to a halt, is to espouse a congressional intent not just to override the Agency's existing statutes but to elevate the quality of data ahead of all the other attributes of its core mission.

These are not abstract questions. Delay costs lives. In 1997, EPA set a new National Ambient Air Quality Standard (NAAQS) for fine particulate matter. After five years of litigation, the federal appeals court for the District of Columbia Circuit has upheld this standard against the last remaining legal challenges to it. *See* Am. Trucking Ass'n v. EPA, 283 F.3d 355 (D.C. Cir. 2002). In issuing a new NAAQS for particulate matter in 1997, EPA estimated that the standard would save approximately 15,000 lives per year. Since that time, the evidence of particulate matter's harmful effects on human health has grown stronger. Even according to EPA's earlier, more conservative estimate of the health risks posed by particulate matter, approximately 150,000 Americans have died due to exposure to particulate matter pollution in the five years since the new standard was first promulgated. This estimate does not include the thousands of cases of nonfatal health effects caused by particulate matter in the five-year period since the new NAAQS was promulgated.

Judicial Review

Despite the wishful thinking of various lawyers representing regulated entities, the Data Quality Act does not provide for judicial review of EPA's determinations regarding the quality of data it uses to support its decisions, except arguably in the context of already-established provisions set forth in the Administrative Procedure Act and all of the federal environmental statutes. There are two reasons for this conclusion:

the doctrine disfavoring repeal by implication and the courts' determined commitment to forego review of any activity other than "final agency action."

It is black letter law that the chief objective of statutory interpretation is to give effect to legislative will. To achieve this goal, courts must take into account tacit assumptions underlying legislative enactments, including not only general policies but also preexisting statutory provisions. Kelly v. Robinson, 479 U.S. 36, 44 (1986) (explaining that courts consider preexisting law in interpreting a new statute). In accordance with this objective, the Supreme Court has upheld for well over 200 years the bedrock principle that "repeals by implication are not favored." Hagen v.Utah, 510 U.S. 399, 416 (1993); United States v. Tynen, 78 U.S. 88, 92 (1870). To achieve repeal of a preexisting statute, Congress must either make an explicit statement that the second piece of legislation repeals existing law or create a second law that flatly contradicts the first. Hagen, 510 U.S. at 416; Passamaquoddy Tribe v. Maine, 75 F.3d 784, 790 (1st Cir. 1996).

The Data Quality Act does not provide for judicial review and nothing in its minimal legislative history suggests that Congress intended to create a "right" to data quality enforceable by "affected persons" that overrides other, well-established avenues for judicial review. Therefore, the Data Quality Act cannot be read either to repeal the judicial review provisions contained in the Administrative Procedures Act and EPA's authorizing statutes or to create a "second law" that contradicts these other, preexisting statutes. For all of these reasons, it is extremely unlikely that a court would accept an aggrieved party's effort to read in such an intent.

Yet even if the Data Quality Act is somehow read to enable judicial review of decisions made with respect to pieces of data by covered agencies, it is an equally well-established principle of administrative law that judicial review is only appropriate in the context of "final agency action" and interlocutory appeals of data quality issues during a rulemaking or other proceeding would almost certainly be rejected.

The Supreme Court laid out a two-part test in *Bennett v. Spear* to determine whether action is considered "final" under the APA: does the action mark the consummation of the agency's decision-making process and does the action determine any rights, obligations, or legal consequences? 520 U.S. 154 (1996). The Court has further held that the proper test to determine whether any rights, obligations or legal consequences are implicated is whether the agency action had a direct and immediate effect on the day-to-day operations, whether the action assumed the status of law, and whether automatic compliance was required. FTC v. Standard Oil, Co., 449 U.S. 232 (1980).

As EPA acknowledges, the actions it takes in response to the guidelines are not in and of themselves binding on any of the parties to a rulemaking until the Agency completes the rulemaking, at which time all participants have ample opportunity to challenge any rule that relies on or incorporates the contested data. *EPA Draft Guidelines*, 1.1. Because the interlocutory denial of a request to correct data does not affect a party's right to challenge such subsequent decisions, EPA is not imposing any new responsibilities on the party without affording the party substantive or procedural due process. Armstrong v. Manzo, 380 U.S. 545, 552 (1965).

Blocking interlocutory appeals under the Data Quality Act is an essential way to preserve judicial economy, give agencies adequate time for reflection, and avoid piecemeal, unnecessarily disruptive review. In some hyper-technical sense, every decision rendered by an agency is "final" for that particular hearing. The Supreme Court has rejected such a reading, holding that allowing interlocutory appeals regarding each particular aspect of a decision might well produce no attainable end to the administrative process. Int'l Tel. & Tel. Corp. v. Local 134, Int'l Brotherhood of Elec. Workers, 419 U.S. 428, 442 (1975).

The Supreme Court has further emphasized that early review of non-final agency action can become unnecessary upon the completion of the agency process, wasting

judicial resources unnecessarily. FTC v. Standard Oil Co., 449 U.S. 232, 242 (1980). Allowing parties to run to court every time they feel aggrieved by an interlocutory data quality decision "improperly intrudes into the agency's decision making process [and] squanders judicial resources since the challenging party still enjoys an opportunity to convince the agency to change its mind." Ciba-Geigy Corp. v. EPA, 801 F.2d 430, 436 (D.C. Cir. 1986). Similarly, the Ninth Circuit has emphasized that if there is the possibility of an initial agency action being reversed or modified during the administrative process, that initial action is not judicially reviewable. Yuk Yu Ma v. Reno, 114 F.3d 128 (9th Cir. 1997). The *Yuk Yu Ma* court added that throughout the administrative process, the agency should feel free to be able to change its mind and consider alternative information. 114 F.3d at 131.

Forcing agencies to act on data correction requests before they have decided whether to rely on the information, and compelling courts to review those decisions, would impose an analogous waste of resources. The decision to deny a data correction request is not an unequivocal decision until the rulemaking is concluded and the agency has the ability to look at the information in a broader context, and in light of other comments on the information, perhaps rendering a different decision.

The Double-edged Sword of Data Quality Act Appeals

While efficient administration of the Data Quality Act is essential and will provide the best outcome for public health and the environment, NRDC cannot forego the opportunity to point out the double-edged nature of the sword now being brandished with such enthusiasm by Jim Tozzi and his allies. Tozzi's web site, http://www.thecre.com/quality, contains three revealing examples of how this campaign could so easily backfire on industry -- and on OMB, if it is not careful.

First, in an extraordinary attempt to make a proverbial silk purse out of a sow's ear, Tozzi extols the possibilities represented by the adverse decision in Tozzi v. HHS, 271 F.3d 301 (D.C. Cir. 2001) where the Court upheld a decision by the National Toxicology Program to upgrade the status of dioxin from a "reasonably anticipated" to a "known" human carcinogen. Brushing aside the Court's embrace of traditionally deferential standard that applies to such technical decisions, Tozzi and his allies claim that the decision will open the flood gates to judicial review of similar decisions by EPA and other agencies.

Ironically, NRDC agrees with Tozzi that EPA has made fatal missteps in writing toxicological profiles by embracing and relying upon fatally flawed and, in some notable cases, "proprietary" (or secret) industry data concerning the chemicals' toxicological effects or exposures. We have attached to these comments three documents explaining notorious recent incidents of such data distortion.

The first is an article entitled *Bad Science* that was authored by NRDC senior scientist Linda Greer and attorney Rena Steinzor and appeared in the *Environmental Forum*. The article explains how industry managed to browbeat EPA into downgrading its toxicological profile of vinyl chloride on the basis of flawed data that was inapposite to the issue of the chemical's toxicity. NRDC believes that this decision constitutes final agency action and would be reviewable under provisions and standards of review in existing administrative law. Obviously, if Tozzi and his allies are correct that the Data Quality Act contains a new cause of action giving aggrieved citizens the right to challenge data quality outside the context of review of the underlying final action, NRDC or others could present the vinyl chloride matter to a judge before the toxicological

profile was written. The judge in that case would confront not a well-reasoned agency decision, but a compilation of flawed data that does not meet any reasonable standard of reproducibility.

A second egregious example of EPA's over-reliance on flawed and, in this case, partially secret data, is the Agency's pending decision to downgrade the toxicity of butadiene, a common toxic chemical contained – among other things – in diesel fuel. See attached NRDC Comments dated June 15, 2001. Industry has apparently convinced the Agency to accept epidemiological studies without releasing the underlying data that would confirm whether the exposure estimates used to predict health consequences are sound. Once again, it is difficult to see how such a process would survive judicial challenge under the Data Quality Act, which – as OMB continually stresses – demands that data relied upon by the government be both "transparent and reproducible."

The third example is a set of comments NRDC scientists and lawyers filed with EPA on March 8, 2002, with respect to use of the secret, allegedly proprietary use of the Calendex model to perform a Cumulative Risk Assessment of the organophosphorus pesticides. The Calendex model was used to calculate the probabilities of exposure to pesticides from food, water, and residential use. On the basis of this secret model, EPA further decided whether to examine exposures from each of the pesticides in various media (e.g., food, drinking water, soil, airborne particles). NRDC believes that use of this secret model may well have systematically underestimated levels of exposure, exposing the public – especially farm children – to grave danger. And, once again, under Tozzi's theories, pending decisions to set tolerance limits on the basis of such secret information should not escape what would almost certainly be very skeptical judicial

review. It is worth noting in this regard that should EPA continue to rely on such secret industry data when it makes its final decisions, NRDC believes that the Agency faces significant legal problems under the provisions of the Food Quality Protection Act and laws other than the Data Quality Act.

Finally, we note an example of the use of confidential business information to support an effluent guideline for the paper industry promulgated under the Clean Water Act. EPA used industry cost data showing that bankruptcies would be caused by an allegedly stringent standard, but refused to make that information publicly available. Despite a challenge by the National Wildlife Federation seeking disclosure of the supposedly confidential business information for the purposes of judicial review, the D.C. Circuit refused to order its release. At the end of the case, the Court upheld the Agency's final decision to embrace the weaker standard, relying in part on the "confidential" information about its costs. National Wildlife Federation v. EPA, 286 F.3d 554 (D.C. Circ. 2002) Once again, if the Tozzi theory is right, both the interlocutory decision refusing to compel EPA to disclose the data, as well as the final decision to uphold the rule, could be appealed directly to court, perhaps delaying the effluent guidelines but also removing – correctly in our view -- any possibility that EPA would give credence to confidential business information submitted in support of any rule or other final agency action.

During the NAS Workshop on data quality, Professor Richard Pierce observed that the Data Quality Act, and the guidelines it spawns, will have "many more unintended effects than intended effects." (NAS Workshop # 1 Transcript at 175) As the Center for Regulatory Effectiveness prepares for battle, we hope that EPA and the constituencies

that are directly affected by its decisions resist these efforts to use the law to wreak chaos that may tie up rulemaking, but will also destabilize government processes that responsible business interests rely upon to conduct their affairs

Modest Improvements to the Draft Guidelines

Although NRDC generally supports EPA's approach to the central issues posed by the Data Quality Act, we hope the Agency will consider making the following additions to further streamline its implementation of the guidelines and to preserve its ability to achieve its statutory mandates without needless and unwarranted delay.

Time Limits for Data Correction Requests

EPA should establish deadlines for requests to correct data and petitions to reconsider such requests, as other agencies and departments have done in their guidelines to implement the Act. We recognize that the Agency faces a difficult task in determining how to set deadlines with respect to information that was first disseminated before the Act became effective. Affording the public some concrete time period to register those objections – six months would be fair – would be a reasonable exercise of the Agency's administrative discretion. With respect to new information disseminated following the Act's effective date and the issuance of EPA's final guidelines, a shorter time period – such as three months – should prove adequate. Without such deadlines, the Agency runs the risk that it will waste considerable resources back-tracking over decisions that must be made at all stages of the decision-making process as information is "newly discovered" by interested parties.

Designation of Influential Information

To the maximum extent possible, EPA should wait to designate information as

"influential" until either a data correction request is made or a final agency action is taken. As Elaine Stanley explained so vividly in her remarks at the first NAS Workshop, establishing a comprehensive system for improving data quality consumes enormous resources. NAS Workshop #1 Transcript at 145-55. Because EPA has such an excellent track record and because of the threats that have been made to misuse the Data Quality Act to further "ossify" its decision-making, we urge that it continue its existing programs without making any attempt to designate information as "influential" under the Act, until and unless it receives a data correction request or it decides to rely on data in taking final agency action.

Public Comment on Data Correction Requests

NRDC urges EPA to establish a procedure allowing the public to comment on data corrections requests for data that are considered central to a rulemaking or other final agency action before the Agency accepts or rejects the correction request. This approach is consistent with the approach followed under the Freedom of Information Act, where EPA gives the submitter of information that is subject to a request for disclosure the opportunity to show why the information should be withheld. Allowing others to challenge efforts that have the effect of suppressing information not only would prevent unwarranted discarding of such data, but would serve to deter the submission of poorly supported requests in the hopes that harassed EPA staff will succumb to such pressure without investigating the allegations fully.

Criteria for Frivolous Requests

EPA has adopted reasonable criteria for deeming requests for correction "frivolous," but should consider clarifying that prior rejections of similar requests are

also grounds for deeming a request frivolous. *EPA Draft Guidelines,* 5.4. NRDC assumes that EPA might conclude that repeated requests to correct the same data are made in "bad faith" or are "duplicative," "burdensome," or "disruptive to the orderly conduct of the action. However, by explicitly providing for the application of relevant precedents, EPA would appropriately place the onus of tracking others' efforts to challenge data on the party seeking to achieve correction.

Content of a Data Correction Request

EPA should expand its requirements for the information that must be included in a data correction request. *Draft EPA Guidelines* 5.2 Specifically, all such requests should state (a) the reasons why the person or organization submitting the request is an "affected person" under the Act ; (b) the reasons why dissemination of the information at the time of the request will cause fairly traceable, concrete injury; (c) how the dissemination of the disputed information would affect that person or organization's legal rights or interests; and (d) whether to the submitter's knowledge EPA has ever acted upon a similar request. All of this information should be readily available to submitters and should provide significant assistance to EPA in implementing the Act.

It is worth noting in this regard that the Data Quality Act is not only an "unfunded mandate" for EPA, but also a potentially enormous burden for the states and tribes that provide the majority of EPA data and information. Thus, EPA is protecting not only its own ability to implement environmental programs effectively, but also the ability of resource-starved partners who do the lion's share of permit writing and enforcement. Embraced opportunistically by industry in other contexts, devolution in the context of the Data Quality Act should not mean obstruction of the states' and tribes' legitimate efforts

to honor their own statutory mandates.

Clear Statement Regarding Effect on Other Laws

The final EPA Data Quality Guidelines should include a clear statement that that nothing in the Data Quality Act or the Guidelines themselves shall be construed to amend or repeal any other statutory obligation of EPA, including deadlines to complete reports, issue rules, or take other actions. Such a clear statement is important so that EPA staff are given the clear message that the guidelines and Data Quality Act did not amend the other laws and cannot be brandished by industry or others as a rationale to ignore the Agency's statutory mandates.

Treatment of the Toxic Release Inventory and Similar Databases

In its *Draft EPA Guidelines*, EPA ducks the important question of whether information it presents as part of the Toxic Release Inventory ("TRI") is covered by the Data Quality Act, opining on one hand that "information generally includes material that EPA disseminates from a web page," and, on the other hand, that "information prepared or submitted by an outside party" is only covered when EPA distributes it in a manner that suggests that "EPA endorses or agrees with it." *Draft EPA Guidelines*, 1.1 ***NRDC strongly recommends that the Agency exclude TRI from the coverage of the Act, lest the Agency sink without a trace in a morass of complaints about the quality of data provided directly by industry. Similarly, other EPA databases, such as the Safe Drinking Water Information System, also simply present data prepared and submitted to EPA by outside parties.***

The Act requires that agencies establish "administrative mechanisms" for the correction of information that is "maintained *and* disseminated" by the government. FY

2001, Consolidated Appropriations Act, P.L. 106-554, Section 515 (b)(2) (B) (emphasis added). While it is generally true that anything posted on the worldwide web is "disseminated" in the most public of ways, OMB has taken care to circumscribe the application of the Data Quality Act to such materials by providing that agencies only "disseminate" information when they adopt it as their own or otherwise endorse its content. *Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies; Reproduction (OMB Guidelines)*, 67 Fed. Reg. 8452, 8545 (Feb. 22, 2002) [hereinafter *OMB Guidelines*]. This interpretation is crucial to the sensible implementation of the Act, creating what could be termed a "conduit" exception: agencies serving merely as conduits for third party information need not assume the plainly insupportable burden of fact-checking that information. With respect to TRI data, EPA clearly lacks the resources to confirm the accuracy of each piece of data. To open the door in this context to possible self-serving claims by one company that information provided by another company is inaccurate or incomplete, and therefore that such information should be pulled down from the worldwide web, would pervert the clear intent not only of the Data Quality Act but the Emergency Planning and Community Right to Know Act, as expanded by the 1990 Clean Air Act Amendments.

In the category of unintended consequences, NRDC urges EPA and OMB to consider that if TRI is deemed covered information under the Data Quality Act, then it is also likely that all of the financial reports and other filings kept by the Securities and Exchange Commission would be subject to the Act. The prospect of investors and others filing a series of data quality challenges before the SEC and other government financial

institutions should make any general counsel pause to reflect on the meaning of "maintain and disseminate" in this context.

Peer Review, Risk Assessments, and the Safe Drinking Water Act

According to OMB's *Guidelines* advising agencies and departments how to implement the Data Quality Protection Act, information must be "objective." *OMB Guidelines*, 67 Fed. Reg. at 8458. Further, information meets this threshold requirement when it is "accurate, reliable, and unbiased." Id. at 8459. OMB adds that to meet these criteria, agencies and departments must use "sound statistical and research methods regarding scientific, financial, or statistical information," in turn defining such "sound" methods as those that use the data quality principles applied by Congress to risk information that is used and disseminated pursuant to section 1412(b)(3)(A) and (B) of the Safe Drinking Water Act (SDWA). Id. at 8460.

To put it mildly, NRDC and other public interest representatives were quite surprised at this effort to import the standards established under one of EPA's authorizing statutes into the large number of statutes that govern agencies and departments with such widely disparate missions as protecting public health and safety, collecting taxes, and conducting the nation's defense. OMB's demand that agencies and departments "adopt or adapt" the SDWA standards goes beyond any colorable interpretation of its authority under the Data Quality Protection Act. ***Accordingly, we commend EPA for its refusal to universally adopt the narrowly-applicable SDWA standards, but remain deeply concerned about what even the adaptation of the SDWA provisions could mean to both the Agency's fulfillment of its core mission and its overall implementation of the Data Quality Act.***

The SDWA provides that, in making decisions under a single, specific provision of the Act, "*to the degree that an Agency action is based on science*," the Administrator shall use "the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices." This provision further requires that EPA disclose certain information about the risk assessments conducted under this single, specific provision, including the "upper bound or lower bound estimate of risk." 42 U.S.C. 300g-1(b)(3)(A) (emphasis added)

OMB's effort to incorporate the narrowly-applicable SDWA standards into the Data Quality Act is extraordinarily dangerous because it implies that the performance of a risk assessment is "scientific" and that the results of a risk assessment must control EPA (and other agencies') decisions, as opposed to the standards and mandates contained in preexisting authorizing statutes. By refusing to acknowledge the uncertainties that make risk assessment more of an art than a science, OMB uses the Data Quality Act to advance its agenda of pushing agencies to perform *quantitative* risk assessment, and not mere *qualitative* analysis, creating the unfortunate illusion that decision-makers can make judgments on how to apply the precautionary principle and other statutory mandates on the basis of precise, "factual," numerically-based data.

Under this regime, quantitative risk assessment would serve as a self-contained decision tree, with two added twists. If the risk assessment determines that the risk is small, rather than erring on the side of caution, we would refrain from acting. If the assessment demonstrates a significant risk, then the system should move to the stage of risk management, where compliance costs are brought into play. The precautionary principle and other statutory mandates appear at the end of the gauntlet, as a value to

guide us with respect to risks that have survived these other analyses. This sequence effectively repeals crucial provisions of the Clean Air Act, the Clean Water Act and other EPA authorizing statutes, which deal with scientific uncertainty in a very different manner.

In contrast to OMB's enthusiastic embrace of "scientific" risk assessment, NRDC believes that risk assessments should instead be viewed as tools used by agencies to make decisions on a mixture of facts, science, and policy considerations. In contrast to OMB's mischaracterization of risk assessment as factual "data" that is "scientific" and "objective," risk assessment should serve merely as a device for organizing a wide range of information that is then subject to statutory mandates. Risk assessors should do their best, in the face of uncertainties at all stages of the process, to describe *qualitatively* the characteristics of the risk. Decision-makers should consider this information and determine whether to act in the face of scientific uncertainty, as Congress clearly intended EPA to do when it passed the Agency's authorizing statutes.

All versions of risk assessment methodology for toxic chemicals consider the quantity and content of a release of the chemical, its fate and transport through the environment, the levels of exposure experienced by people and ecosystems, and the consequences that may result from such exposures. Three types of uncertainty plague every stage of such analyses: we lack data, we lack technology, and we lack science.

Data gaps suffuse the regulatory system; at their simplest level they mean that we lack adequate information about the quantity, chemical characteristics, and toxicology of

even the most common pollutants.[1] The situation has become so embarrassing that the chemical industry has launched an unprecedented testing program to fill some of these blank spaces, although it remains to be seen whether those results will garner widespread acceptance as scientifically sound.[2]

Second, we either lack or have failed to implement technologies capable of monitoring the odyssey of common toxic chemicals through dynamic environments.[3] Not only do we have an inadequate system of monitoring, especially water quality monitoring, but we remain remarkably ignorant about how climate changes and other physical phenomena (e.g., building down-wash) affect transport of pollution and therefore its fate.

Third, we do not understand the synergistic and cumulative effects of such emissions, much less the biological mechanisms by which they cause cancer and other debilitating diseases. EPA efforts to conduct more research in these areas should be a much higher priority.

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[1] In a recent report covering 2,863 organic chemicals produced or imported in amount above one million pounds annually, EPA concludes that there is no toxicity information available for 43% of such chemicals and that a full set of basic toxicity information is available for only 7%. *EPA Analysis of Test Data Availability for HPV Chemicals*, 22 Chem. Reg. Rep. 261 (1998).

[2] Sara Thurin Rollin, *Chemical Safety: C9ommercial Labs, Consultants Ready for Influx of Requests for HPV Testing*, 58 DAILY ENV=T REP. A-5 (1999) (describing the voluntary testing program organized by the American Chemistry Council on behalf of its members).

[3] *See, e.g.,* Michael P. Vandenbergh, *An Alternative to Ready, Fire, Aim: A New Framework to Link Environmental Targets in Environmental Law,* 85 KY. L. J. 806, 812-14 (1997) (explaining that surprisingly few assessments of the state of the environment in the United States are available).

Because of the gaps inherent in the risk assessment process, which plagued EPA long before "risk assessment" became a term of art in the regulatory lexicon, and because Congress was concerned about the social and economic impact of regulation, authorizing statutes never direct the Agency to regulate exclusively on the basis of scientific considerations. Instead, Congress and the Executive Branch have assumed for 30 years that qualitative considerations, as well as hard, quantitative science, must inform the regulatory process.

For example, the Clean Air Act instructs EPA to protect public health with an "adequate margin of safety." 42 U.S.C. §7409(b)(1)(2002). Many other environmental laws require the Agency to explore the possibility of less damaging alternative products or practices and to consider the cost of pollution controls before mandating them. Commanding agencies to wait until science is certain about every possible salient fact would mean decades of delay, flouting provisions of many laws and regulations that set deadlines for action in response to the risks of toxic exposure.

As for OMB's efforts to use the Data Quality Act to require that agencies apply peer review to virtually every decision, NRDC once again urges EPA to avoid what could easily become an overwhelming hurdle for routine regulatory decisions. EPA already has in place both an institutional entity – the Science Advisory Board – and a methodology for performing peer review and, while NRDC has argued in other contexts that the Agency must implement significant reforms of that process, the Data Quality Act does not require EPA to establish procedures that duplicate those that already exist. For an explanation of NRDC's position on peer review, see the *Bad Science* article attached to these comments.

Since Dr. Graham's appointment as director of OIRA, OMB has repeatedly exhorted agencies to use peer review much more widely, suggesting that peer reviewers disclose potential conflicts of interest and sources of bias, but never demanding that these disclosures be made public. See, e.g., *Draft 2002 Cost Benefit Report*, 67 Fed. Reg. 15014, 15019 (Mar. 28, 2002). OMB instructs agencies like EPA to select peer reviewers on the basis of their "expertise," without providing that peer review panels be balanced and free of members who have clear conflicts of interest. (Id.)

As EPA already knows, a crucial purpose of peer review is to ensure that research is conducted in an intellectually honest and scientifically appropriate manner and that the results claimed by the researchers are supportable by the data they generate. To permit others to make these judgments, scientists must stand ready to disclose their underlying data, even if the results of a study were not what they – or the sponsors of their studies – had hoped or anticipated.

Scientists participating in peer review panels should disclose to the public – and not just to government officials -- all sources of potential conflicts of interest and bias, including financial benefits, specific grants, and other forms of institutional support. Scientists are expected to have opinions. If scientists with a financial stake in the outcome of a scientific inquiry participate, the objectivity of the review is immediately suspect. Candidates with a conflict of interest should not serve on a panel except under the most unusual circumstances: i.e., they are the only ones who have essential expertise on the subject being reviewed.

In sum, EPA should pursue ongoing efforts to improve the objectivity and transparency of peer review, without succumbing to OMB's exhortations that it employ

this expensive procedure every time it makes a decision and that it select peer reviewers without regard to bias.

We hope that you find these comments helpful and appreciate the opportunity to submit them.

Respectfully submitted,

Rena Steinzor,
Academic Fellow,
NRDC and
Professor
University of Maryland School of Law

Jennifer Mogy,
Legal Intern
NRDC

cc: OIRA Director John Graham, EPA Assistant Administrators Steven Johnson and Paul Gilman

ATTACHMENTS:
Bad Science Article
Butadiene Comments
Organophosphorus Pesticide Comments

June 15, 2001

William H. Farland, Ph.D.
Office of Research and Development
U.S. Environmental Protection Agency
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Room 41225
Mail Code 8601-D
Washington, DC 20460

By Messenger

Dear Dr. Farland,

The Natural Resources Defense Council (NRDC), a non–profit organization with more than 500,000 members dedicated to protecting public health and the environment, is writing to express our grave concerns about the recent EPA Health Assessment of 1,3-butadiene (EPA/600/P-98/001B January 2001 Consensus Review Draft). Although we commend you and your staff for the excellent analysis that led you to conclude that butadiene is a known human carcinogen, we believe that this work will be for naught in view of the assessment's reduction in the unit cancer risk estimate (potency estimate) of butadiene. Contrary to EPA's analysis, we believe that the data support a *more* stringent potency factor than the existing 0.25/ppm estimate, not a less stringent one. We address our primary concerns here and hope you will take these comments into account and modify your reassessment of butadiene potency to better incorporate standard scientific practices and better protect public health.

Our concern with butadiene stems in large part from the very widespread and substantial extent to which the general public is exposed to this compound. Women, children, the elderly, and the infirm all breathe in butadiene daily. EPA's recent groundbreaking work that estimated the risks associated with toxic air pollution (the Cumulative Exposure Project, or CEP) found butadiene to be the single biggest risk driver of all hazardous air pollutants in the U.S. Further compounding NRDC's concern is the fact that several of the key cancers associated with exposure to the compound – for example, leukemia and non-Hodgkins lymphoma (according to human epidemiology studies) and mammary/breast cancer (according to data from laboratory animals) – are on the increase in this country. It is quite possible that these cancers are being caused by the widespread and continuing public exposure to butadiene.

Furthermore, there is much at stake in the decision to mistakenly downgrade this compound's toxicity. EPA is in a position to lower butadiene and other toxic chemical emissions from vehicles as it develops its mobile source strategy and as it considers options for replacing MTBE in gasoline recipes. A wrongful downgrading of butadiene's potency will inevitably lead to minimal EPA concern for its emissions and will undoubtedly lead to increased air concentrations

in the near future. Practical options for continuing to limit and reduce releases of butadiene into the environment will not have a chance to be developed if the compound drops from the country's list of priority concerns.

You thus face a real possibility of failing to substantially decrease exposure to a known human carcinogen on a flawed "wishful thinking" analysis of a toxicity data set full of holes.

We plead with you to take an especially precautionary approach to setting a "safe" level of human exposure to butadiene, to err on the side of safety when considering the data available to inform your decision, and to not be lulled into thinking that your data set is adequate to justify this dangerous downgrade in the compound's toxicity. We urge you in the strongest possible terms to re-consider if there really is a sufficient basis at your fingertips to allow increased widespread public exposures to a chemical that you have determined is a known carcinogen.

The epidemiological evidence for butadiene is insufficient to serve as the exclusive basis for setting the potency factor for this compound

It is EPA's position that it is generally preferable to use high-quality epidemiologic data, when available, over toxicologic data for quantitative risk assessments. We agree. The problem has been that such high quality epidemiology studies can seldom be done. EPA believes that in this case one particular study (Delzell 1995) is of sufficient quality as to present an opportunity to update its toxicologic risk assessment with its findings. NRDC disagrees completely.

EPA recognizes in several places in its document that in general there are serious problems with the exclusive reliance on epidemiological data for its decision-making and that in particular there are serious limitations with the Delzell study. The problem is, once having listed these problems, the Agency proceeds to not take them seriously. It is as though once recognized, the problems go away. Unfortunately, merely listing them does not eliminate their impact on EPA's deliberations; it merely underscores the flaws.

Exposure concentrations estimated by Delzell are not sufficiently accurate, and EPA has insufficient data to understand how they were constructed

EPA's belief that Delzell's work (particularly as modified by Health Canada) can be used as a sole basis for its risk assessment appears to be based largely on its determination that the study's exposure estimates are sufficient to allow the determination of a valid and accurate dose response curve (p 10-1,3). We do not agree. Delzell's estimates were perhaps an improvement upon previous estimates (and perhaps not), but they are still far from sufficient to warrant the confidence that they have engendered. Her estimates were not based on actual exposure measurements, for example, and could not begin to take into account such important determinants of exposure as the frequency and duration in which a worker undertook particular specific tasks, the distance of an operator from an emission source of butadiene, the frequency and intensity of emissions during certain days of the year, etc. Rather, the authors relied on a model of work histories abstracted from personnel records. Delzell herself states "exposure estimates developed...are imprecise assessments of the exposure levels experienced by any individual worker", that "misclassification of exposure levels is likely", and that "only limited efforts were feasible to estimate a range of credibility for the exposure estimates" (Macaluso, Delzell et al, 1996). The authors further concede that their procedure lacked extensive validation because of budget constraints (Ibid).

As a general matter, there are problems with accurately quantifying exposures in epidemiological studies, especially because many exposures happened decades ago. Butadiene presents an acute case of the problem of estimating exposures because EPA finds itself relying on **a single industry study** with serious acknowledged limitations in the accuracy of the exposure estimates it used (Delzell 1996 and an additional analysis of the same data by Health Canada); other epidemiological studies that exist suffer from more serious limitations and in many cases did not even attempt to quantify butadiene exposures. Furthermore, to the best of our knowledge, EPA has never looked at the actual raw exposure estimates for the workers who succumbed to leukemia in the Delzell study, relying instead on the already cumulated totals in aggregate form. As a result, the Agency is hamstrung; it cannot assess the methods used to stratify the individuals into different exposure bands, account for the distribution of exposures that occurred within the band, or understand the impact of different stratification schemes of the raw data on the analysis. We urge that the Agency review in detail these critical individual exposure calculations, the methods by which they were produced, and the methods used to create exposure. It is also essential that you make them publicly available for review before placing undue reliance on a single product of work.

It should not escape anyone's attention that the one study which serves as the primary basis for the Agency's risk estimates was prepared under contract for the International Institute of Synthetic Rubber Producers, an organization with a clear stake in the outcome. This potential conflict of interest should serve as further justification for your own hard and detailed examination of into its raw data components and the methodology used by the study's authors.

As always in epidemiology, one worries about concomitant exposures to other chemicals that may confound the observed relationship. EPA discusses possible confounding by exposure to other industrial chemicals (e.g., dithiocarbamates and styrene) at some length and believes they are not significant here. However, it glosses over the fact that the Delzell study **did not stratify for smoking**, a critical problem in any epidemiological study examining cancer as a primary outcome. A cancer epidemiology study that fails to control for smoking would be seriously criticized by most scientists as flawed and confounded; such a study should not serve as the definitive single basis upon which to regulate this important chemical.

Finally, misclassification of exposed versus unexposed populations is also given some attention, and EPA concludes (again, we believe, without having looked at the raw data itself) that problems of worker misclassification are minimized in the Delzell study. However, it glosses over a serious and unique situation with butadiene, which is that **no one is unexposed**. That is, since butadiene is present in significant concentrations in ambient air, there is no adequate "unexposed" control group. In this case, misclassifying exposed persons as unexposed would serve to mask the relationship between exposure to butadiene and leukemia- thereby leading to an erroneous conclusion that the exposure caused fewer outcomes than it actually did. Again, this problem alone should provide sufficient justification to the Agency to consider additional data in its determination of a potency factor for butadiene.

For the reasons detailed above, we do not believe that the Delzell exposure analysis is of sufficient quality to allow EPA to use it as the sole basis of a new potency estimate for butadiene. Perhaps more importantly, we have identified three fatal flaws in Delzell's study, independent of its methods of estimating exposures, any one of which alone should steer EPA away from relying on this work as a basis for its decision; taken in total, the three major flaws discussed below provide an overwhelming basis for EPA to reject the use of this study to re-determine the potency of this important compound.

Fatal Flaw One: Using only mortality data, and discounting morbidity, results in an underestimation of risk, and of potency

First and most seriously, in relying on Delzell, EPA concerns itself only with leukemia ***deaths*** (mortality) and not with leukemia incidence (morbidity), as this was the only endpoint studied. That is, the Agency doesn't count workers who are sick with cancer, only those who die during the study observation period, with leukemia listed as the cause of death on the death certificate. This is scientifically faulty, and results in an assessment that is not public health protective.

Five year relative survival rates for leukemia by year of diagnosis among whites is 44% and among blacks is 31%. Thus, well over one-third of persons with leukemia die of other causes. It is a cancer that is treatable, or controllable, by modern medical interventions. Thus, by only including persons who die of leukemia, this epidemiology study greatly underestimates the risk of cancer caused by butadiene exposure. Because the Agency's unit cancer risk estimate relies solely on this human study, this puts into question the final assessment.

Fatal Flaw Two: Failing to account for deaths after the age of 70 results in an underestimation of risk, and of potency

The study upon which EPA relies does not include leukemia deaths in workers or former workers over 70 years old. This is a gross error; of 20,148 deaths from leukemia in the U.S. population in 1995, 59% of persons died at or over the age of 70 (11,907 deaths). Leukemia has a latency period of 10-20 years, making it a virtual certainty that many of the workers in the human epidemiology study used by the Agency died after the cut-off point of data collection. In a cruel irony, such workers not only represent uncounted deaths, but also they would be counted as exposed people that did not die of leukemia. The result is a dramatic underestimation of risk. Standard occupational epidemiological practices demand that workers be followed beyond their employment years for at least the length of the latency period of the disease in question. This study did not follow basic epidemiological practices, and should be considered in that light.

Fatal Flaw Three: Basing the unit cancer risk estimate on a study using only leukemia as an endpoint disregards its potency as a multisite carcinogen, and results in an underestimation of risk, and of potency

All of the animal data on butadiene suggest that it is a multisite carcinogen. In mice, the most sensitive endpoint is the lung, and females are more sensitive than males. The human study that the Agency relies upon ignores these sensitive parameters. Perhaps even worse, the Agency is ignoring epidemiological evidence that raises serious concerns about human cancers other than leukemia, particularly the excess of non-Hodgkins lymphomas (NHL) observed in butadiene polymer production workers that is discussed at length in Chapter 8 of the document. Although EPA notes that researchers have been unable to find an association between NHL mortality and cumulative exposures, they conclude that it may be peak exposures (for which no data are available) rather than cumulative exposures that caused these excesses. In light of such evidence suggesting a relationship between butadiene and NHL, EPA's failure to consider NHL in its unit cancer risk estimate is inexcusable.

Despite this excellent summary of information and good matching of the "Hill criteria" to the butadiene/NHL link (p. 8-12), EPA mysteriously drops its concern about this second important cancer when it develops its potency factor in Chapter 10, relying instead exclusively on leukemia for its calculations. EPA compounds its error by neglecting other cancers as well; the Agency

does not account for the fact that the Delzell (1995) study reported a "slight" increase in lung cancer among maintenance workers, and increased deaths from cancer of the large intestine and larynx.

Although difficulties in exposure estimations for NHL and small numbers of other cancers might preclude EPA from setting its potency factor based on this disease, these issues should serve as a "red flag" warning that more is at issue with butadiene than leukemia. The additional cancers thus strongly suggest that the current epidemiological data base on butadiene is not yet sufficiently developed for EPA's risk assessment determinations.

Selection of a linear model to calculate potency is not a conservative or public health protective choice for this compound

EPA's errors in relying exclusively on the Delzell epidemiological study are compounded by the exposure-response modeling that it undertakes to develop the final potency estimate. Four different forms of the relationship between the relative rate (RR) of leukemia death and measurement of exposure were evaluated by Delzell, and subsequently Health Canada added a fifth form (a modification of Delzell's "square root" model to a "shape" model). Estimates of risks and exposure levels corresponding to levels of risk of interest ranged by several orders of magnitude depending on the model used, particularly at low levels of risk which are of greatest concern for the general population. For example, EPA reports that the 10^{-6} risk level for exposure to butadiene ranged from 0.2 ppb in the linear model to 10^{-7} ppb based on the shape model. All the models fit the data "adequately," according to EPA. Clearly, as EPA acknowledges (p 10-8) the final risk estimates based on extrapolation procedures are highly dependent on the choice of model.

It is in the selection of the model to use that EPA most obviously fails to err on the side of safety when setting a potency estimate for butadiene, for it does not select the model that leads to the most protective estimate. Instead, it selects the linear model, stating that there is "no compelling reason" to deviate from the linear model historically used for human data.

Let us suggest a compelling reason to the Agency. For all the reasons stating above, NRDC believes there is no rational reason for the Agency to rely on one absurdly narrow epidemiological study to estimate the risk of butadiene to the general public. If it nonetheless moves forward and uses the study anyway, EPA has a responsibility to select the most protective of the "adequate" models -- given that it faces critical gaps in the information it has relied upon in the first place to fit the data to any model at all. When setting "acceptable" exposure levels for a known human carcinogen with widespread and substantial public exposure, EPA should select the most protective model.

Use of a 3X adjustment factor is grossly inadequate to compensate for gaps in the epidemiological data for butadiene and possible errors in model selection

The Agency recognizes the need for an adjustment factor to account for underestimating the extra cancer risk from exposure to 1,3-butadiene. It suggests that a 3X factor will "address concerns that the leukemia risk estimate from a male worker population may underestimate total cancer risk to the general population" (Assessment, p. 11-7). However, 3X is in no way sufficient to address the use of an all-male worker population with one identified health outcome to derive a safety factor for the general population.

Butadiene is a compound where we have considerable data suggesting disproportionate sensitivity of females. In rats, females show much greater production of the highly mutagenic metabolic product diepoxybutane than males, and female rats have increased incidence of mammary tumors from exposure to butadiene. As EPA acknowledges, breast cancer rates are increasing in women of all ages in the US, and the known risk factors explain only a small proportion of the occurrence of breast cancer. Yet EPA has no epidemiological basis upon which to derive a number that will protect women from the risks of exposure to this compound. By choosing to base its number only on human male mortality from leukemia, EPA turns its back on the fact that animal data suggest reduced butadiene exposure would be particularly important for the protection of women.

In addition, butadiene is linked with leukemia, and leukemia is one of the most common cancers in children. Thus, as the Agency recognizes (p 8-15) there is a clear basis for concern that exposure to butadiene may be an additional risk factor increasing the leukemia risk further in children. Children breathe more liters of air per pound of body weight than adults and often spend more time outdoors. Thus, they are disproportionately exposed to this chemical and deserve a wide margin of extra protection.

Where critical data gaps exist, such as where EPA has only animal data and needs to develop a protective standard for human exposure in setting an RfD, it is generally EPA policy to apply two ten-fold safety factors – 10X to account for species-to-species variability and 10X to account for variability among individuals – for a final 100X safety number. Where there are gaps in information about disproportionate sensitivity to children, the Food Quality Protection Act in analogous situations requires that an additional 10X safety factor be applied as well. Since EPA lacks **any human data** to develop safe levels of butadiene exposure for women and children, and it has considerable animal data to suggest that females, at least, may be particularly sensitive to the compound, and children may be disproportionately exposed in the general population, EPA should not rely exclusively on epidemiological evidence for its potency calculation. However, if it does, we believe that a 1,000X safety factor, or another methodology that accounts for all these knowledge gaps, is justified. The addition of such safety factors to EPA's flawed potency estimate of 0.01/ppm would raise the potency figure to 10 per ppm.

Summary: This Assessment must be adjusted to reflect the serious limitations of the human study used to estimate the potency of butadiene

The above concerns are extremely serious, and demonstrate that reliance upon this otherwise excellent Health Assessment will in fact result in an increased public health risk. If these errors are not corrected by 1) incorporating the excellent body of animal data demonstrating the carcinogenic potency of butadiene, 2) changing the model selected for assessing the data, and 3) incorporating an adjustment factor that appropriately and realistically reflects data gaps and uncertainties, the resulting Health Assessment will be seriously flawed, as will the important future regulatory decisions that rely upon it.

We look forward to a timely response to these comments as soon as you and your staff have had an opportunity to digest them. If there is additional information about your decision that you believe would allay some of our concerns, we will be very happy to review it or meet with you to discuss the material.

Thank you so much for considering these comments. Butadiene is perhaps the most important toxic chemical in our nation's air, and we hope you will act in a protective manner for the public in your deliberations on this compound.

Sincerely,

Jennifer Sass, Ph.D.
Linda Greer, Ph.D.
Jon Devine

cc: Aparna M. Koppikar, Mail Code 8623-D

March 8, 2002

Public Information and Records Integrity Branch (PIRIB),
Information Resources and Services Division (7502C),
Office of Pesticide Programs (OPP),
Environmental Protection Agency,
Ariel Rios Bldg., 1200 Pennsylvania Ave., NW.
Washington, DC 20460.

Docket control number OPP-34250

Re: Comments on the preliminary Cumulative Risk Assessment of the Organophosphorus Pesticides, released December 3, 2001

Submitted by the Natural Resources Defense Council

These comments are submitted in writing to the above address, and electronically to: opp-docket@epa.gov

Federal Register: December 28, 2001 (Volume 66, Number 249)] Page 67249-67250

Dear Sir or Madam:

We submit the following comments on behalf of the Natural Resources Defense Council (NRDC). NRDC uses law, science, and the support of more than 500,000 members nationwide to protect the planet's wildlife and wild places and to ensure a safe and healthy environment for all living things. NRDC has no direct or indirect financial or fiduciary interest in the manufacture or sale of organophosphate pesticides.

Many of these comments were presented, in much the same form as in this document, to the Scientific Advisory Panel (SAP), February 5, 2002 in spoken form, and in written form for distribution to SAP members. In addition, a copy of those comments is available in the docket (Docket control number OPP-00756).

Unless otherwise noted or referenced, all page number references in the text of these comments refer to the preliminary Cumulative Risk Assessment (CRA) of the Organophosphorus Pesticides, released December 3, 2001.

SUMMARY OF PRELIMINARY OP-CRA

Under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act (FQPA), EPA must reassess existing legal limits (called tolerances) for pesticide residues in food to ensure that they meet a stricter new safety standard. In particular, EPA may only establish a tolerance for a pesticide chemical residue in or on a food if EPA determines that the tolerance is "safe." 21 U.S.C. § 346a(b)(2)(A)(i). A tolerance will meet this requirement only if "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." Id. § 346a(b)(2)(A)(ii). The health-protective standard of the FQPA requires EPA to give special consideration to the health of infants and children, and EPA must "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue." Id. § 346a(b)(2)(C)(ii)(i). Most importantly for present purposes, tolerances must be set at a safe level when one considers exposures to the chemical itself as well as cumulative exposures to the chemical and any other pesticide with which it shares a common mechanism of toxicity.

The preliminary CRA represents a first step in making sure that tolerances for the OPs, which share a common mechanism of action, are safe when cumulative exposures are included. EPA has concluded previously that the OPs all act similarly – by blocking the activity of an enzyme in the brains of animals and humans. The process by which the OPs act is known as acetylcholinesterase inhibition; simply put, these pesticides are neurotoxins. Accordingly, the law requires EPA to determine how toxic these related poisons are when they act in concert (a hazard assessment) and further requires EPA to quantify people's cumulative exposures to all of the OPs (an exposure assessment). The hazard assessment and the exposure assessment are combined into an overall estimate of risk.

Before turning to our concerns, a brief overview of EPA's methods is in order. First, in its hazard assessment, EPA focused on the inhibition of cholinesterase as the common mechanism of action, and in doing so chose an index chemical -- methamidophos -- to use to compare the degree of cholinesterase inhibition that each of these pesticides exhibited. Second, the Agency makes a number of important assumptions in creating its exposure assessment. They are listed in summary form below:

- *General:* EPA used a calendar-based program called Calendex™ (a proprietary model developed by Novigen) to calculate probabilities of exposure from food, water, and residential use. In addition, EPA decided -- based on its assessment of where residues were likely to appear -- whether to examine exposures from each of the OPs in various media (food, drinking water, etc.). The letters following the names indicate in which assessment(s) they appear, food (F), water (W), residential (R):

acephateF,W,R	ethopropF,W	phorateF,W
azinphos-methylF,W	fenamiphosF,W,R	phosoloneF
bensulideW,R	fenthionR	phosmetF,W
chlorethoxyfosW	malathionF,W,R	phostebupirimW
chlorpyrifosF,W	methamidophosF,W	pirimiphos methylF
chlorpyrifos-methylF	methidathionF,W	profenofosW
diazinonF,W	methyl parathionF,W	terbufosF,W
dichlorvos	mevinphosF	tetrachlorvinphosR
	naledW.R	tribufosF.W

(DDVP)F,W,R dicrotophosW dimethoateF,W disulfotonF,W,R	oxydemeton-methyl (ODM)F,W	trichlorfonR

- *Food:* The food assessment is national in scope, but OPs were excluded from the food assessment if they have been voluntarily canceled, if they have only residential or public health uses, or if EPA concluded that they have no detectable residues in food. Data sources for food residues included the U.S. Department of Agriculture's (USDA) Pesticide Data Program, USDA's Continuing Survey of Food Intake by Individuals, the Food and Drug Administration (FDA) Total Diet Study, and FDA monitoring data

- *Drinking Water:* The assessment incorporates regional exposures from residential and drinking water sources, as the most appropriate way to account for the considerable variation in potential exposures across the country. People generally obtain drinking water from local sources, and there are different pest issues in different regions, so the use of pesticides varies in different parts of the country, as well as seasonally, requiring a more localized approach. Data sources for the water component include the USDA Agricultural Chemical Usage Reports, data from USDA indicating typical planting and harvesting dates for field crops and fresh market and processing vegetables, available local sources of information, monitoring studies from the U.S. Geological Survey, and other sources. EPA also used a computer modeling program called PRZM-EXAMS/IR, supplemented by water monitoring data. (The Pesticide Root Zone Model (PRZM) calculates what happens to a pesticide in a farmer's field on a day-to-day basis. It considers factors such as rainfall and how and when the pesticide is applied. EXAMS II assesses the fate, exposure, and persistence of pesticides in aquatic ecosystems. The Index Reservoir (IR) is representative of a number of reservoirs in the central Midwest. These models provide a basis for assessing potential of pesticides to contaminate water.)

- *Residential:* For the residential assessment, EPA examined data from surveys and task forces (e.g., National Home and Garden Pesticide Use Survey), special studies and reports from the published scientific literature, its own Exposure Factors Handbook, and other sources, including the State Cooperative Extension Service.

SUMMARY OF NRDC COMMENTS

NRDC commends EPA for the progress made in the last two years in developing and refining its OP cumulative risk methodology. EPA's OP-CRA has come at the expense of an at least two-year delay in meeting statutory deadlines for tolerance revisions and has required an enormous investment of agency resources. Dozens of scientists and several organizations have also invested thousands of hours of effort into the dozens of meetings, conferences, special studies and advisory committee meetings focusing on the OP-CRA.

Empirical results from the then-current OP-CRA released in December 2001 confirm that cumulative OP exposures and risks among infants through age one and among one to five year olds are excessive, even without factoring in the need for a 10-X FQPA safety factor. We believe strongly that the Agency is now positioned to reach definitive conclusions regarding those specific uses of individual OPs that account for the largest shares of dietary risk among infants and children.

Moreover, as the OP-CRA Monte Carlo-based methodology and databases have been improved over the last several years, the same list of OP-crop combinations continues to emerge at the top of the list in terms of shares of dietary exposure and risk. No past model refinement or database enhancement has substantially changed the ranking of OP-food combinations at the top of such lists, nor is there any reason to project that future methodological refinements will make much of a difference. Accordingly, it is time for EPA to begin crafting and implementing appropriate risk mitigation measures on the few dozen OP-food uses accounting for the largest share of risk.

While further improvements can and should be made in the OP-CRA methodology and in the databases supporting the methodology's applications, the time has come for the agency to move ahead with risk mitigation actions targeting the relatively small number of clear and unequivocal OP food use risk drivers. This is the only way for the public to begin realizing tangible benefits from its already-significant investment in the OP-CRA process.

We look forward to future work by EPA to fold the n-methyl-carbamate insecticides into this CRA model, since these insecticides clearly share a mode of action with the organophosphates and clearly will pose a significant combined risk to children once these risks are assessed together. Our reasons for believing that the N-methyl carbamates and OP's should be dealt with in one cumulative risk assessment are detailed in comments submitted by NRDC previously (Sept 4, 2001). Briefly, the N-methyl carbamates and the organophosphate pesticides share: a common mechanism of action; a common toxic profile following exposure; a common, highly variable, range of toxic potencies; and a common profile of use, and thereby a common exposure risk profile. Clearly, the science supports grouping of OP's and N-methyl carbamates together.

The Agency must recognize the many areas of the OP-CRA, which systematically underestimate exposure, or underestimate risk, many of which are discussed in detail in these comments. NRDC recommends strongly that the Agency incorporate these necessary changes, most of which were supported by the Scientific Advisory Panel (SAP meeting, February 5-8, 2002). Without these corrections, the OP-CRA will not adequately protect the US population, and will therefore not legally meet the requirements of the FQPA. In this case, the Agency must acknowledge this shortfall, and apply uncertainty/safety factors sufficient to provide a margin of safety for the US population, including fetuses, infants, children, and the elderly.

NRDC recommends to EPA the following improvements to the preliminary OP-CRA, which will improve the scientific credibility of the CRA, and more adequately protect fetuses, infants, and children, the intended targets of the FQPA:

To improve the scientific credibility of the CRA, the Agency must quantitatively incorporate information from the "open" published literature. This is essential to any risk assessment, including this OP-CRA, because:

- consideration and appropriate incorporation of the published literature provides a state-of-the-science assessment

- all toxicology data used in this CRA to determine relative potency factors (RPF's) came solely from industry studies, all or most are unpublished, which have not undergone public scrutiny and peer review

- chemical manufacturers which perform toxicity studies of their own chemicals have a financial interest in the study outcome which may result in attempts to nullify results, both by study design, and by data reporting

- the published literature provides a rich database upon which to assess OP toxicity, and is incorporated into these comments where appropriate, to demonstrate the scientific basis for the concerns raised herein

EPA must adequately consider fetuses, infants, and children as an especially vulnerable group, and apply an FQPA factor of at least 10-fold, because:

- all toxicology data is derived from studies on adult animals, not fetuses or juveniles
- DNT testing is still outstanding for most OP's, and because some OP's have been shown to be fetotoxic in DNT testing
- it is scientifically justified to consider all OP's to be developmental neurotoxic chemicals
- the Agency has not considered data on regional brain effects, behavioral effects, learning and memory effects, reproductive effects, immune effects, cancer, and others
- EPA has not incorporated data for highly exposed children, such as children living on farms or whose parents are farm workers, and has not incorporated child, infant, and fetus-specific data for water, non-dietary, and other exposures. NRDC has previously identified these deficiencies to EPA, but the Agency to date has ignored our pleas (see attached petitions: (a) a Directive that the Agency Designate Farm Children as a Major Identifiable Subgroup and Population at Special Risk to Be Protected under FQPA; and (b) a Directive that the Agency Consistently Fulfill its Duty to Retain the Child-Protective Tenfold Safety Factor Mandated by the FQPA).

EPA must consider all age groups, including 0-12 months, and 7-19 years age groups:

- because each of these age groups form a vulnerable sub-population, with distinct dietary and activity behaviors, and must be considered under the law

EPA must augment the CRA where exposure has been systematically underestimated, as follows:

- consider toxic degradates
- include violative residues, both those which are illegal because no tolerances exist, and those which exceed allowable limits
- include additional OP's, and a more complete set of OP uses, where current use patterns are likely to lead to significant exposures among certain population groups, including mixers-loaders and applicators, children of farm workers, or other people likely to be exposed as a result of where they work or live
- assess water exposure scenarios, not by considering typical use rates and use patterns, but rather by assessing peak exposure scenarios, which are likely of significant risk to exposed populations
- include non-agriculture sources of OP's in the water assessment
- consider the seasonal peaks of residues associated with food and drinking water

EPA must amend the CRA where vulnerable populations have been ignored, as follows:

- use the BMD_{01}, rather than the less protective BMD_{10} to determine the point of departure (PoD) for the risk assessment

- consider not only the magnitude, but also the duration, of cholinesterase inhibition

- consider farm children as a high-exposure population, deserving special consideration

- correlate peak exposure times with eating patterns, so that risk of eating fruit or vegetables with high residue levels is modeled, and these consumers are protected

- account for "leftover" scenarios, where a high residue food is consumed for an extended period of time

To better understand, and respond to uncertainty in the method and databases supporting the CRA, the Agency must:

- perform sensitivity analyses to evaluate the impact of model assumptions

- develop uncertainty distributions to capture population variability in exposure levels and patterns, and, in biological responses to a given exposure scenario

- determine what a tolerable level of inhibition is in a fetus, a neonate, and a juvenile. In the absence of such data, incorporate an estimate of uncertainty into the risk assessment.

- determine uncertainty in the relative potency factor (RPF) determination; determine how well they fit the toxicological data; how well they fit acute, subchronic, and chronic data; and how well they fit adult versus fetus, and neonate data

- determine if certain ethnic groups, and their eating patterns, are under-represented in the food consumption data (PDP data), and correct the impact of any possible bias on the risk assessment

To validate and further refine the risk assessment, EPA must:

- use CDC biomonitoring data, NHANES data, and data from the published literature to evaluate the model predictions, to "truth test" the model with real-world data

- quantitatively compare behavioral and developmental alterations, and other clinical endpoints, with cholinesterase inhibition

- compare the impact of various BMD values (01, 05, 10 was suggested by the SAP), and justify the final choice

- indicate where clinical effects or morphological alterations occur in the absence of detectable inhibition of cholinesterase activity

EPA must take steps to better characterize the shape of the distribution of exposure curve since it is neither appropriate nor defensible for EPA to simply assume a uniform distribution. Such an assumption presumes that each value has an equal probability of occurring. This is not an accurate assumption. On an ongoing basis, EPA must:

- make a better attempt to characterize the shape of the distribution of exposure more accurately

- use a log-normal skewed distribution, when appropriate, in order to capture the extreme cases

EPA must discard the "rolling window" model, which artificially reduces variability, and thus does not capture real-world risk

- EPA's approach averages exposure over several days, in an exposure model known as the "rolling window". This approach artificially reduces variability by averaging peak exposures out over time, thereby artificially increasing the margin of error (MOE) estimates. This approach is less sensitive to high-level exposures that may occur in the population.

EPA must use at least two models, at least one of which is non-proprietary, for all assessments, and refuse to rely upon a model that is not accessible to the public

- EPA cannot rely exclusively upon a proprietary (i.e. confidential and non-public) model. Proprietary models are by definition unscientific -- the calculations cannot be replicated by outside researchers or scientists, and cannot therefore be subjected to public scrutiny and peer-review. It is absolutely unacceptable to expect the public to blindly trust the accuracy and reliability of a model developed for regulated parties, and that purports to provide information critical to defining risks from pesticide exposures. We demand complete access to the assumptions and calculations built into this secret model. Without complete transparency we can only assume the worst: that the model was designed with embedded assumptions that favor the industries that supported the model's development, rather than designed to protect children, the elderly, and sensitive populations. Use of a secret model is contrary to all of the agreements EPA made with stakeholders to improve the transparency of the regulatory process and is likely to be illegal as well.

OVERARCHING CONCERNS

The Agency must appropriately incorporate information from the published literature on OP toxicity

In this CRA all toxicology data upon which the relative potency factors (RPF's) are based has been provided by the chemical manufacturers, and is unavailable in the public domain. These studies have not undergone peer review, and are not available for public scrutiny; without this they lack scientific credibility as the scientific community defines it. Moreover, and as discussed in more detail below, the risk assessment model used in this CRA, Calendex™, was developed without public input or scrutiny, and therefore suffers from a similar lack of scientific credibility. NRDC is concerned that this process reveals an alarming trend of government abdicating its responsibility to protect public health and the environment. It is to be expected that the corporations producing toxic chemicals will seize upon all available opportunities to influence the governmental regulatory process.

Dr. Marcia Angell, senior lecturer at Harvard Medical School, and former editor-in-chief of the New England Journal of Medicine, defines a financial conflict as any financial association that may cause a researcher to prefer one outcome over another. Financial conflict, Dr. Angell points out, is a function of the situation, not the investigator's response to it; there is nothing "potential" about it. Her working definition of financial conflict is applicable to scientific research such as the toxicology studies submitted by chemical manufacturers to the Agency, and used in this CRA.

Most concerning, the Agency has not made any serious attempt to incorporate into this CRA the scientific knowledge of OP toxicity which is freely available in the published literature. This rich

database remains virtually untapped by the Agency, and thus NRDC is convinced that this CRA cannot be said to represent the current scientific understanding of OP toxicity. NRDC demands that the Agency incorporate, in a quantitative and meaningful way, the published literature on OP toxicity (such as those cited in this document), or make appropriate adjustments for this omission through the use of safety/uncertainty factors.

I. CHILDREN ARE INADEQUATELY CONSIDERED: EPA must apply an FQPA factor of at least 10X

Under the Food Quality Protection Act's precautionary approach to protecting children, EPA must maintain an additional 10-fold margin of safety in its risk assessments for individual pesticides to "take into account potential pre– and post–natal developmental toxicity and completeness of the data with respect to exposure and toxicity to infants and children." 21 U.S.C. § 346a(b)(2)(C). EPA can use a lower margin of safety "only if, on the basis of reliable data, such margin will be safe for infants and children." *Id* The organophosphorus pesticides are designed to interfere with cholinergic stimulation, which has been shown experimentally to be essential for normal nervous system development. Even transient interference with the cholinergic system during development produces permanent structural and behavioral damage(*2-4*). The following paragraphs detail the scientific and legal justification for an FQPA safety factor of at least 10X.

I.A All toxicology data are derived from adult animals: disease data cannot be extrapolated to fetuses, neonates, and juveniles

It is an extremely serious omission in this CRA that all toxicological assessments, including dose-response determinations, are based solely on adult animals (cholinesterase inhibition in female rat brain), with no experimental data from fetuses, neonates, or juveniles. Considering that the impetus of the CRA is the FQPA, which mandates the re-evaluation of pesticide exposure with specific attention to the effects on fetuses, infants, and children, it is an obvious, egregious omission to disregard these life stages in the toxicology assessment. This omission is enormous, especially in light of the fact that less than half the OP's have undergone developmental neurotoxicity testing (DNT) as required by the Agency. The focus on adults is pervasive throughout the CRA, and is therefore discussed throughout these comments.

It is well established in the scientific literature that the body is extremely vulnerable to chemical assault during development of target organs and systems. During neural development the nervous system is acutely vulnerable to neurotoxic assault, and exposures may result in long-term or permanent destruction or dysfunction. This is equally true for the developing immune system, endocrine system, and reproductive system. Data from adult animals cannot adequately describe the risk to fetuses, infants, and children without the application of an uncertainty factor to provide an adequate margin of safety to protect people during these especially vulnerable developmental stages.

On Feb. 7, 2002 the SAP addressed the question of exposures to immature animals and humans. Dr. Patrick Durkin (Syracuse Environmental Research Associates, Inc.) asked the question, "where are the kids?" He voiced concern that all the relative potency factors (RPF's) are based on adult toxicology data, in spite of data demonstrating that some OP's, such as malathion, are substantially more toxic to neonates than to adults. Dr. Durkin supported NRDC's comments on this topic, and demanded that this issue be addressed by EPA in the CRA. In the same context, Dr. Durkin objected to the focus on toxicology studies submitted by registrants, and suggested that the Agency also consider the published literature. Noting that it has been known for years that some OP's are more toxic to neonates than to adults. Dr. Durkin reiterated that RPF's that are based on neonate data

must be incorporated into this risk assessment. No dissenting views were voiced at the SAP, and NRDC encourages the Agency to take seriously this concern.

I.B. Developmental toxicity testing (DNT) is still outstanding for most of the OP's: this critical data gap makes it impossible to assess the neurotoxic effects to fetuses, infants, and children

Studies show that developmental neurotoxicity (DNT) testing is more sensitive, and therefore more appropriate for protecting children's health. DNT testing is essential for pesticides, not only as a measure of toxicity to the developing brain and nervous system, but also as an often more sensitive measure of developmental and reproductive effects generally. EPA's 10X Task Force recommended that "developmental neurotoxicity testing be included as part of the minimum core toxicology data set for all chemical food-use pesticides for which a tolerance would be set[1]. Former EPA Assistant Administrator Lynn Goldman, M.D., highlighted this recommendation in presenting the Task Force report to the SAP in December 1998.

At the SAP meeting of Feb. 5, 2002, Dr. Jean Harry (NIEHS) commented that the DNT battery of tests was much more rigorous than the EPA normal battery of toxicological testing, and was much more appropriate for assessing developmental neurotoxicity.

In its draft Policy on *Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process,* issued May 10, 1999, the Office of Pesticide Programs acknowledges that "the developmental neurotoxicity study, in particular, is capable of identifying adverse effects not evaluated in other test systems and that the data might lead to lower NOAELS and RfDs." Based on this important knowledge, OPP further acknowledged in this policy document its intent to add several additional toxicity studies to its core or Tier 1 toxicology requirements for registering new pesticides, including the developmental neurotoxicity study (as well as the acute neurotoxicity study in adult rats and two immunotoxicity studies). EPA also vowed to make good on this intent by including such studies by revising to 40 CFR Part 158.

On August 6, 1999, EPA announced its intent to "call in" data from acute, subchronic, and developmental neurotoxicity studies from the registrants of 140 already-registered neurotoxic pesticides[2]. The DCI on September 10, 1999 called in data for 34 cholinesterase-inhibiting organophosphate insecticides. To date, only a handful of the organophosphate DNT and comparative cholinesterase inhibition tests have been received by the Agency[3].

In the absence of DNT results, the Agency is legally obligated to apply an FQPA factor of at least 10X, to provide a margin of safety despite the gaps in the database.

I.C. All OP's must be assumed to be developmentally neurotoxic chemicals

The Agency must presume that the developing nervous system is more vulnerable than the adult to neurotoxic insult. At the SAP meeting of Feb. 5, 2002, Dr. Jean Harry (NIEHS) commented that it is safe to presume that all OP's will be developmentally neurotoxic, supporting NRDC's statement that EPA should presume as much.

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[1] USEPA, Toxicology Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health (draft), 10X Task Force, 11/30/98, p. 11

[2] Federal Register: August 6, 1999,Volume 64, Number 151, page 42945-42947

[3] Sue Makris, EPA, personal telephone conversation with Jennifer Sass, NRDC. February 15, 2002

Presuming all OP's to be developmentally neurotoxic is consistent with current scientific understanding of neurobiology, embryology, and neurotoxicology. A number of individual OP chemicals have been shown to be especially harmful to fetuses, infants, and children, even at low doses(*4-10*). This is expected, given that the OP's are designed specifically to disrupt cholinesterase levels, thereby affecting synaptogenesis, neurite outgrowth (axonal and dendritic), arborization, and kindling. Functionally, this has been demonstrated to result in permanent disruptions in learning, memory formation, cognitive ability, and behavior. Of great concern, the developmental window of vulnerability to chlorpyrifos was very wide, extending from the embryonic period into postnatal life, making it likely that *in utero* exposure will result in irreversible neural damage(*2*).

In his publications, Dr. Slotkin points out that numerous animal studies demonstrate that immature animals are far more susceptible to acute toxicity of chlorpyrifos, despite the fact that they recover from cholinesterase inhibition more quickly than adults(*2*), presumably due to multiple mechanisms of toxicity of chlorpyrifos. These findings were supported by the DNT results, which demonstrated evidence of neuropathology and increased vulnerability of fetuses when exposed to chlorpyrifos (Chlorpyrifos IRED p. 16; Makris et al.[4]). Most concerning, in these experiments neuropathology was seen in the neonates at the lowest dose tested; these studies were unable to identify an offspring NOAEL in the DNT (Chlorpyrifos IRED p. 16-17). Structural alterations in brain development, which would result in permanent brain dysfunction, were seen at the lowest doses tested. Similar increased sensitivity of young animals, compared with adults, has also been demonstrated with malathion in studies performed by the registrant.

Registrant studies submitted to the Agency demonstrate differences in inhibition ranging from 2-fold to over 20-fold, between adults and pups given equivalent doses of malathion[5]. Most dramatic, two hours after a single oral dose of technical grade malathion administered to young adult rats and PND11 pups, the adult brain cholinesterase levels were inhibited 3-4% (male and female), compared with controls. However, brain cholinesterase activity was inhibited in the pups by 81-84% (female and male), compared with controls, a 20-fold difference compared with the adult response. Clearly, these data demonstrate that an FQPA factor of at least 10-fold is required when extrapolating from immature to adult toxicological data, and a factor of 20-fold may be justified in some cases.

The organophosphate pesticides are a common-mechanism group, they target a common enzyme, they induce a common set of effects, and therefore, by all scientific criteria, if any are shown to be fetotoxic, then all should be presumed to be fetotoxic, unless data shows otherwise. Clearly, the OP's that were rigorously tested, using appropriate study designs (such as DNT studies) were shown to be especially harmful to the developing nervous system. The OP's must all be considered to be developmentally toxic, both the parent compound, and the toxic metabolites. NRDC believes that any other conclusion is not supported by the scientific evidence of fetotoxicity demonstrated in DNT studies, and will not adequately protect fetuses, infants, and children.

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[4] Makris S, Raffaele K, Sette W, Seed J. A retrospective analysis of twelve developmental neurotoxicity studies submitted to the USEPA Office of Prevention, Pesticides, and Toxic Substances (OPPTS). Draft 11/12/98.

[5] letter from Cheminova, submitted by Jellinek, Schwartz, and Connolly, Inc. Re: Malathion: Preliminary data from a developmental neurotoxicity study. February 13, 2001. EPA LIN#L0000617. Obtained by NRDC, Jennifer Sass, by FOIA RIN-0283-02

I.D. The CRA failed to consider regional effects, behavioral effects, cognitive effects, learning and memory effects, reproductive effects, and others

The endpoint of all toxicological studies used in this CRA was whole brain cholinesterase activity. This approach ignores regional variability in responses within different brain regions, and masks local perturbations that may be very severe. NRDC believes that histopathological examination would reveal regionally affected brain areas. Chlorpyrifos has been shown to have both cholinergic and non-cholinergic toxicity, the latter through interference with adenylate cyclase cell signaling pathways(*2, 3, 11*). Through the non-cholinergic mechanism, chlorpyrifos elicited widespread neural damage, and disrupted cell development. Through the cholinergic mechanism, chlorpyrifos induced apoptosis during neurulation, resulting in reduced cell numbers in brain regions that are enriched in cholinergic neurons. These regional effects would be undetectable in the toxicology protocols used by the Agency in this cumulative risk assessment.

Behavioral and cognitive testing, including learning and memory tests, reflex tests, and others, are key to assessing the true toxic effects of any neurotoxic and fetotoxic chemicals. Most importantly, with any developmental neurotoxic chemical such as the OP's, effects are the result of more than the magnitude of the dose. Rather, the effect is dependent on the dose, the duration of the effect (cholinesterase inhibition), and the stage of development at which the exposure takes place. Exposures during key windows of susceptibility during neural development, even at very low doses, are most likely to have permanent, devastating effects on neural function, including behavior and cognition. This was never examined in the current CRA, and is a very serious gap in the understanding of the toxic effects of OP's. In particular, the effects of OP's on fetuses, infants, and children have not been adequately described.

Epidemiology studies of farmworkers and people living in agriculture communities suggest that pesticide exposures are associated with numerous diseases, including Parkinson's Disease, non-Hodgkin's lymphoma, leukemia, and brain cancer(*12-27*). There has been no consideration of these data in the CRA. And, none of these disease endpoints have been considered in the toxicology data utilized by the Agency to determine the RPF's or the BMD. Yet, these studies provide strong evidence that exposure to pesticides is of extreme concern at current use rates and use patterns. NRDC is concerned that these findings, freely available in the published literature, have been ignored in this CRA.

In addition to paying attention to sensitive biological endpoints, it is also essential to recognize the value of these physiological systems to the complex integrity of a person. For example, neurotoxic damage resulting in the permanent loss of several IQ points in a lab animal may not even be detectable, yet, will severely limit the potential of a person, or exposed population(*28*). Inability to pay attention, mood changes, inability to predict consequences of actions, and explosive temper are all results of fetal exposure to alcohol(*29*). While these effects might seem subtle, almost negligible, in an animal study measuring crude endpoints such as body weight changes or fetal death, they will cripple the social and emotional potential of an affected human

At the SAP meeting Dr. Richard Bull (MoBull Consulting) stated that the OP's have toxic effects on almost any hydroxylase enzyme, and are therefore likely to have widespread physiological effects. Dr. Bull suggested that the Agency consider reproductive analysis, and other toxic endpoints, in addition to neurotoxic considerations. NRDC supports these assertions, and believes that it is sound science to test for all toxic endpoints, including developmental neurotoxicity, comparative cholinesterase inhibition (between adults and neonates), and reproductive endpoints. We encourage the Agency to include such testing routinely in its future assessments.

I.E. The CRA did not consider newborns, young children, and teenagers

The preliminary CRA did not consider people of ages 0-11 months, 6-12 years, 13-19 years, and over 56 yrs. As a result, and as Dr. Harry observed to the SAP, infants, children, teenagers, and the elderly are excluded from the current CRA. This is a very serious omission, and NRDC believes that it renders this preliminary CRA unable to comment on an exposure or risk to these absent age groups. NRDC believes that these omitted age groups are the intended targets of the FQPA, and without consideration of these groups, the requirements of the FQPA have not been met.

II. EXPOSURE HAS BEEN UNDERESTIMATED

NRDC believes that this preliminary CRA is not a public health protective document. Rather, it is evident that in many ways, exposure, and consequent risk, has been underestimated throughout. NRDC details examples below, demonstrating this document to be an underestimate of exposure, and recommends that EPA amend the CRA appropriately, or the appropriate use of safety/uncertainty factors.

II.A. The Agency did not consider toxic degradates; and downplayed the toxicity of metabolites

NRDC recommends using data on toxic degradates where available, such as some water monitoring and food data. Where such data are not available, the EPA should estimate exposure and risk based on chemical structure, mobility, degradation rate, and other known characteristics of the degradates. Though EPA has abundant data for dietary exposure to OP's, its PDP databases only include monitoring data for residues of the parent compound. Likewise, toxic degradates/metabolites and treatment byproducts were not included in the water assessment. Where metabolites were considered, they were presumed to behave as the parent compound would. This is not scientifically justifiable, and NRDC believes that the omission of proper consideration of degradates results in an underestimation of exposure.

The incomplete consideration of degradates and treatment products was discussed by various members of the SAP, and was considered a glaring omission. Dr. Richards (Water Quality Laboratory, Heidelberg College, Ohio) suggested that, in addition to a more complete consideration of degradates, the Agency should more realistically track OP's in rivers and streams. Dr. Bull supported this sentiment. Dr. Capel (Univ Minnesota) also noted that exclusion of oxons might lead to a significant underestimate of exposure.

Many pesticides, including organophosphate insecticides, have toxicologically significant metabolites and stereoisomers. For example, malaoxon — the bioactivated form of malathion — inhibits acetylcholinesterase about 1,000–fold more strongly than does malathion(*30*). Similarly, EPA acknowledges that dimethoxon, a significant metabolite of dimethoate, is 75-100 times more potent than dimethoate in inhibiting acetylcholinesterase. Moreover, this metabolite is found under field conditions on food crops. The primary degradate of ethyl parathion, paraoxon, is five times more easily absorbed than parathion and 40 to 50 times more toxic. One of the chief metabolites of chlorpyrifos, chlorpyrifos oxon, inhibits cholinesterase more strongly than the parent compound, but appears to be very short-lived. It breaks down to TCP, a metabolite that is much more persistent in blood, and based on a limited sample may be found in the urine of up to 92 percent of children, as was documented in EPA's recently released chlorpyrifos preliminary risk assessment. Compared with chlorpyrifos, TCP is stated to be "more mobile and significantly more persistent in many soils, especially under anaerobic conditions" (chlorpyrifos IRED p.20). Further, the Agency states that,

"upper-bound estimated environmental concentrations of TCP exceeded chronic DWLOCs for children" (chlorpyrifos IRED p. 16). This is especially disconcerting, given the "evidence of increased susceptibility of rabbit fetuses relative to dams", demonstrating increased susceptibility of fetuses, compared with adults (IRED p.16).

The impact of these OP metabolites on developing animals – where even short-lived compounds could conceivably have irreversible effects on the nervous system – heightens the need for prudence in carrying out cumulative assessments. EPA appears to have no requirement for chemical-specific pharmacokinetic studies in fetal animals that would aid in discerning the contribution of toxic metabolites, to children's risk. This omission likely results in a great underestimation of exposure risk in the CRA.

II.B. The Agency did not consider "violative" residues, which may underestimate exposure

To ensure that tolerances are set at a safe level, EPA must account for all pathways of exposure, including exposures from legal and illegal behavior that results in violative residues. These data are available to the EPA, and should be incorporated appropriately. Violative residues may be either residues detected on food for which no tolerance is issued, or which exceed the tolerance. In either case, these are extremely important, and may indicate a widespread and very dangerous problem. If residues exceed the tolerance routinely, seasonally, or even occasionally the CRA must consider these "real world" residues. It is unacceptable for the Agency to disregard these data as "outliers" without providing evidence that they are flatly incorrect or of inconsequential health impact. If these "violative" residues are the result of spray drift, of illegal applications, of machinery residues, etc., they must be considered indicative of widespread exposure and a contributor to cumulative OP risk. In any case, the Agency must provide data as to the frequency, spatial and temporal pattern (if any exists), and magnitude of the "violations". The absence of these monitoring data in this CRA is a considerable data gap, which likely underestimates exposure.

At the SAP meeting (February 5-7, 2002) public commenter Dr. Judy Schreiber, a toxicologist of the NY Attorney General Office, stated that the Agency must include violative residues in any complete CRA. NRDC commented similarly. SAP member Dr. Christopher Portier (NIEHS), stated that the only way that PDP data should discard violative residues is if the food is discarded too, and not eaten.

II.C. The Agency did not include some OP's where use may be of sufficient dose or frequency to post health risks

Any omissions of OP's and OP uses will result in underestimates of exposure in the CRA. When OP's that are actually or potentially present in the environment are omitted from the CRA, an additional safety factor must be applied to adjust for this omission. In this preliminary CRA the Agency has excluded from consideration all chemicals, and all chemical uses, which have been cancelled, voluntarily withdrawn, or phased out. In addition, chemicals that only have public health uses have been excluded, and chemicals that don't have any detectable residues have been excluded. NRDC is concerned that many of the chemicals that are being withdrawn or phased-out will still be exposure threats for years to come. In addition, the phase-out periods, which are already several years, may be extended, thus extending exposure to these "excluded" OP's. People may have private stores of these chemicals for many years to come. Further, NRDC is concerned that emergency and public health uses may be of sufficient frequency and dose, or used in such close proximity to people, as to pose significant risk to exposed populations.

Uses that NRDC believes must be included (or replaced by a safety factor) that were excluded from EPA's risk assessment include:

Public health uses including:

- chlorpyrifos in fire ant mound treatment and mosquito control;
- fenthion in mosquito control;
- naled in mosquito and black fly control;
- phosmet in fire ant mound treatment

OP uses not included because insufficient data was available:

- tetrachlorvinphos (pet shampoos)
- DDVP (flea collars)

OP's not included because they are being phased out:

- ethion
- ethyl parathion
- sulfotepp

OP's not included because they have only public health uses:

- temephos

OP's not included because no residues were detected:

- cadusafos; 1 tolerance on import bananas
- fenitrothion; 1 tolerance on wheat gluten
- temephos; used as a mosquito larvicide
- propetamphos; 2 tolerances, for animal feed and for processed food
- coumaphos; 16 tolerances on meat and meat-by-products. Also on honeybees (over 100 current section 18 emergency tolerances)

NRDC is concerned that many of the uses that are being phased-out will remain on the market for many years, and that their phase-out period may be extended. Others, such as tetrachlorvinphos and DDVP, are currently registered for use on pets, and yet were not included in the probabilistic assessment because the Agency did not have sufficient data on exposure. This is an especially egregious omission since the screening-level assessments for these uses indicate risks are of concern. NRDC is also concerned that temporary tolerances granted for emergencies are not considered in the CRA, and yet pose definite food hazards. For example, coumaphos, an extremely potent OP, is used on honeybees to protect against mites (section 18, emergency). Poor compliance with application procedures by farmers has resulted in coumaphos in honey (CARAT meeting, Jan 16, 2002, discussion with Marcia Mulkey, EPA). And, yet, the Agency does not consider coumaphos, in any use at all, anywhere in the CRA. This is clearly a contradiction, and underestimates exposure to one of the most potent of OP's.

II.D. The water assessment underestimates exposure by modeling only "typical" exposure scenarios, and ignoring peak exposure scenarios that are likely to be of significant risk to exposed populations

NRDC recommends to EPA that the water assessment be based on all available data of use rates, use patterns, and monitoring data where available, so that the CRA will adequately capture the population at highest risk. The water model (PRZM/EXAMS) used for the preliminary CRA plots the distribution of daily residues over multiple years, and plots multiple sites rather than high-exposure sites; no point estimates were considered. This is a major departure from the individual risk assessments, where point estimates were used, to capture the 99.9th percentile. Ignoring peak point

estimates leads to a very severe underestimation of risk, and ignores the potentially devastating effects of exposures of OP's, even at very low doses, and even for short duration, on the developing nervous system. The CRA further underestimates risk by presuming typical use rates and typical use patterns. This is a departure from the individual risk assessments, which assessed exposure based on maximum allowable label rates and maximum allowable use patterns. This more conservative approach, while still ignoring exposures that exceed allowable limits, at least attempts to protect those people who suffer allowable high-end exposures. This CRA makes no such attempt. The final output of the CRA water assessment reflects the typical, or "average" use pattern, which, although describing the majority of the calendar days, does not describe the majority of the risk.

II.E. The water assessment did not consider non-agricultural sources of OP's, which is likely to significantly underestimate exposure

In the water assessment, there is no consideration of urban uses, public health uses, or section 18 emergency uses, of OP's. Inclusion of these would clearly exceed "typical" uses. Dr. Zeisse (Reproductive and Cancer Hazard Assessment, OEHHA, Cal-EPA) noted that pest outbreaks, which lead to higher use rates, were never considered. Several SAP members noted the absence of any contribution to water from non-agricultural sources of OP use, and states that this is non-trivial, and should be considered (Drs. Capel [Univ Minnesota] and MacDonald [MacMaster Univ]). Further, incomplete consideration of oxons may lead to a significant underestimate of exposure, stated Dr. Capel.

II.F. EPA did not consider food purchased at farmers markets, farm stands, "U-Pik" farms, and from household gardens

EPA did not account for the dietary exposure of a significant number of consumers who purchase produce at farmers markets, farm stands, and "U-Pik" farming operations. Over 1.9 million people buy vegetable and fruits from nearly 13,000 farmers, at more than 2,000 community-based farmers markets and farm stands in the US. *See* National Association of Farmers' Market Nutrition Programs (http://www.nafmnp.org/). These consumers include pregnant women, infants, and children, and must be protected. By ignoring this significant community of consumers, EPA vastly underestimates dietary exposure and cannot ensure that exposure to residues at the tolerance level will be safe. Not having the data does not justify ignoring the dietary exposure of potentially millions of consumers to residues of OP's at the tolerance level. EPA must ensure that the legal levels of pesticide chemical residues – the established tolerance levels – are themselves safe. 21 U.S.C. § 346a(b)(2)(A).

II.G. The current CRA model does not incorporate seasonal peak exposures, and is therefore an underestimate of exposure

This issue involves a consideration of the seasonality of pest pressures, of pesticide use, and of eating habits. The inclusion of seasonality in the food exposure assessment was discussed repeatedly during the SAP meeting, with all members agreeing that exposures will peak with peak pesticide-use seasons, and must be considered. The current CRA presumes that the food that people eat is constant throughout the year, with no seasonal pattern, and that the pesticide residues associated with that diet is also constant throughout the year. Since the pesticide residues are determined from PDP data, which results from random market basket surveys, it is most likely to capture "average" residue days, and overlook the "peak" days. These peak days, while not frequent, are certainly of high risk. Further, these peak days are likely to be seasonal, concurrent with times of high pesticide use, and therefore occur routinely, and not randomly.

The omission of seasonality associated with the food assessment is also a serious omission in the water assessment. This is because the water assessment does not consider OP exposure from non-agriculture sources. Therefore, the seasonal peaks in urban pesticide use, residential pesticide use, home garden and lawn pesticide use, and public health pesticide use all contribute to peaks in the water, and none are considered by the EPA. This omission is unacceptable, and results in an underestimation of seasonal peaks in both the food and water supply that are very likely to exceed by far the EPA estimates in this CRA. NRDC, and the SAP, urge the Agency to include these seasonal uses, and to consider their seasonal peaks, in order to more adequately assess real-world exposure scenarios.

III. THE CRA IGNORES THE MOST VULNERABLE POPULATIONS: THE EFFECTS OF EXPOSURES THAT MAY BE OF LOW PROBABILITY, BUT OF HIGH RISK IMPACT ARE EXCLUDED FROM THE CRA

III.A. Use of central estimate (BMD_{10}) will underestimate risk unacceptably: use of a BMD_{01} is more protective, and is supported by the data

NRDC recommends using the BMD_{01} rather than the BMD_{10}, to more adequately protect all populations. The point of departure (PoD) of each chemical's dose-response curve was determined to be the BMD_{10}, the benchmark dose where cholinesterase activity was reduced by 10%. The use of the BMD_{10}, a central estimate, rather than its lower limit, ignores risk for those who are most sensitive to cholinesterase perturbations, such as fetuses, infants, and children, for whom changes less than 10%, or sustained changes, may induce permanent alterations in cytoarchitecture of the nervous system. The Agency has never performed a proper evaluation of subtle, sustained, or regional neural responses to OP exposure, either in the adult or in the developing nervous system. Thus, NRDC believes that the choice of a central estimate, which the Agency's own data indicates is higher than the NOAEL points for oral, dermal, and inhalation exposure routes, is a potentially large underestimate of risk. In fact, the BMD_{10} is a full three-fold higher than the dermal NOAEL (1.B p. 40). NRDC believes that use of a lower limit estimate, BMD_{01} is a more appropriate estimate of a PoD, and would better reflect the low-dose exposure scenario, and thus be more health protective.

This issue was discussed by the SAP (Feb. 5, 2002), and it was agreed that the PoD is similar in concept to a No-effect level (NOEL), in that it defines a level of exposure below which there is no effect. NRDC therefore believes that our request for use of a BMD_{01} to define the PoD is more appropriate, and more protective, since it more closely approximates a No-effect level. Dr. Christopher Portier (NIEHS) requested that the Agency show results comparing several BMD values, and suggested a BMD_{01}, BMD_{05}, and BMD_{10} set. Upon questioning by the SAP, the Agency stated that they had never compared the results of the chosen BMD_{10} with another BMD value, and had never done a sensitivity analysis. Dr. Portier encouraged the Agency to do this, and NRDC supports this request.

NRDC has concerns regarding use of the "expanded" model by the Agency to model the animal toxicological data. This model was proposed by R. Sielken under contract to the ACPA (American Crop Protection Agency), and presented to the SAP in December 2001 by Sielken. This model uses the BMD10 instead of the slope (m) to "flush out" the low dose end of the curve, and examine whether a "shoulder", i.e. threshold exists at low dose exposures. The Agency demonstrates, using this model, that only eight of the 29 OP's demonstrate a low-dose "shoulder", demonstrating that, for the majority of the OP's there is an effect on cholinesterase activity at the lowest doses tested. This is an important observation, and supports NRDC's position that use of a BMD_{01} is more appropriate than a BMD_{10}, evidenced by effects of OP's at even the very lowest doses.

III.B. The Agency has measured the magnitude, but not the duration, of OP exposure

NRDC recommends including data on duration of cholinesterase inhibition, in addition to magnitude, to more accurately capture the toxic effect of OP exposure. To measure the full toxic potency of any chemical, including the OP's, it is necessary to measure the effects of sustained duration of exposure. This has not been done in the Agency's model of toxic effects. While the animal toxicology studies considered the magnitude of cholinesterase inhibition at each dose, there was no consideration of the duration of the inhibition. Without any attempt to capture the sustained inhibition of cholinesterase activity, this model is inadequate, and will likely underestimate risk. NRDC encourages the Agency to pursue a truly "expanded" model, which will describe not only the magnitude, but also the duration of enzyme inhibition at each dose. Clearly, a toxic effect that is brief versus a toxic effect that is sustained is not likely to produce the same biological reaction. To disregard the effects of sustained, long-lasting inhibition of cholinesterase (hours, days) is not scientifically justifiable, and will not capture the full toxic effects of exposure to cholinesterase inhibitors. The effects of long-lasting cholinesterase inhibition will be especially important in describing the sensitivity of the developing nervous system to acute and sustained perturbations of cholinesterase activity.

III.C. Farm children are especially vulnerable to pesticide exposure, and are not adequately considered in this CRA

Farm children should be deemed to comprise an especially vulnerable population, and their exposure to pesticides must be considered in establishing tolerances where data is available. Children who live on or near farms are at risk from airborne pesticide drift when they spend any time outdoors. Pesticides sprayed outdoors may enter houses and concentrate in indoor air. Protection of children necessitates routine, consistent monitoring of ambient air pesticide levels in agricultural regions. In this risk assessment, EPA failed to consider available information concerning the sensitivities and exposures of this major identifiable subgroup of consumers.

The children of farmers, farmworkers and agricultural communities – including over 500,000 children under the age of six – are surrounded by a virtual sea of pesticides(*31-34*). They come in contact with pesticides through residues from their parents' clothing, dust tracked into their homes, contaminated soil in areas where they play, food brought directly from the fields to the table, and contaminated well water. These children are likely to have the highest exposure to pesticides of any group of people in the country. Furthermore, farm children often accompany their parents to work in the fields, raising their pesticide exposures even higher. Many of the children with the greatest pesticide exposures are from migrant farmworker families, who are poor and usually people of color or recent immigrants.

Children who live on or near farms are at risk from airborne pesticide drift when they spend any time outdoors. Fog samples gathered in suburban Maryland and in agricultural regions of California revealed up to 16 different agricultural pesticides. The pesticides detected included organophosphates, triazines, dinitroaniline (pendimethalin), and chloroacetanilides (alachlor, metolachlor). The levels of organophosphates and their oxygen analogues often exceeded 10 μg/liter: two or three orders of magnitude above levels reported in rain. The maximum measured level of the highly toxic parathion oxygen analogue (paraoxon) was 184 μg/liter – a level considered sufficient to cause significant cholinesterase inhibition. In addition, volatile, fat-soluble pesticides were found in fog at concentrations far greater than expected(*35*). Pesticides sprayed outdoors may

enter houses and concentrate in indoor air. A Minnesota study revealed that an application of two herbicides by ground-broom sprayer 50 meters upwind from a farmhouse resulted in a three- to four-fold elevated concentration of both chemicals in outdoor air adjacent to the farmhouse, and a 50% increase in the concentration of one of the herbicides inside the farmhouse. The herbicide in indoor air was attributed to infiltration of outdoor air.[6] Outdoor air concentrations of pesticides in agricultural regions may be extremely significant from a public health perspective. This is likely particularly true for pesticides applied via fumigation or broadcast spraying. Children who live in agricultural regions may receive significant airborne pesticide exposures when playing outdoors. Infiltration of homes by outdoor air may also result in airborne exposures inside the home. Protection of children necessitates routine, consistent monitoring of ambient air pesticide levels in agricultural regions. Because overexposures to organophosphates and soil fumigants have been documented, these categories of pesticides should receive particular scrutiny.

Epidemiology studies of farmworkers and people living in agriculture communities suggest that pesticide exposures is associated with numerous diseases, including Parkinson's Disease, non-Hodgkin's lymphoma, leukemia, and brain cancer(*12-27*). There has been no consideration of these data in the CRA. Yet, these studies provide strong evidence that exposure to pesticides is of extreme concern at current use rates and use patterns, especially to farmworkers and their families, and agricultural communities.

At the SAP meeting several members stated that the failure of this CRA to address agriculture communities and being especially vulnerable to high pesticide exposure is a very serious oversight. Consideration of these communities would include populations that live near agriculture areas, farm families, and effects of spray drift. In addition, one SAP member pointed out that considering protective clothing should also include a consideration of what happens to the clothing after the pesticide application. Does it sit on household furniture, does it sit in a laundry room, or hang in a back porch? These scenarios are real possibilities, particularly in agricultural communities, and are not included in this CRA. This will likely lead to an underestimate of exposure among farm families.

III.D. Level of regulation must ensure a reasonable certainty of no harm for ALL fetuses, infants, and children: allowing tens of thousands of children to be unprotected is inadequate (the so-called 99.9TH percentile policy).

Under the FQPA, EPA must ensure that there is a reasonable certainty of no harm through exposure to pesticide chemical residues. 21 U.S.C. § 346a(b)(2)(C). If the best evidence suggests that thousands of children will exceed the reference dose for a pesticide, EPA is barred by statute from finding a reasonable certainty of no harm to these particular infants and children, and the Agency may not issue a tolerance at that level. EPA may not sacrifice the hundreds or thousands of children who may exceed the reference dose for a particular OP. Under FQPA, the burden is upon the advocate of a tolerance to prove (and upon EPA to find) that there is a reasonable certainty that no children will be harmed in EPA 's pesticide decisions. Thus, if the best evidence suggests that hundreds or even thousands of children will exceed the reference dose for an OP, EPA is forbidden by statute to find a reasonable certainty of no harm to these particular infants and children, and the Agency should not issue a tolerance at that level. EPA seeks to mask in this approach the fact that even regulation at the 99.9th percentile, for a pesticide commonly used on a ubiquitous children's food, means that 0.1% of all American children under age six (around 24,000 children in all) could exceed the chronic RfD every day, based on the best information available to the agency. Further, a child exposed to multiple organophosphate pesticides may fall within the 99.9th percentile for one,

[6] Camann D, Geno P, Harding H, Giardino N, Bond A, al. e. A Pilot Study of Pesticides in Indoor Air in Relation to Agricultural Applications. Proc Indoor Air 1993; 2:207-212.

but lie above the safety threshold when cumulative OP risks are calculated. No reading of the statute will support any approach that allows hundreds or thousands of children to exceed the reference dose. Regulating dietary residues of OP's at the 99.9th percentile directly violates the plain statutory language of the FQPA.

III.E. The current CRA does not correlate peak exposure times with eating patterns

NRDC recommends that the EPA evaluate the seasonality of food residues. It is important to consider the overlap of peak residue periods (likely to be seasonal) with peak eating patterns, such as eating fresh fruit shortly after pesticide applications that give rise to elevated exposures. These data are available to the EPA, and should be considered. These very real exposure patterns are not "random", but have clear seasonal patterns, and are likely to result in high dietary exposures. This issue is of particular concern for young children, whose eating patterns are likely to correlate with seasonal fruit availability. That is, children may eat much more of a fruit when it is in season and therefore less expensive and readily available. This time period is also when pest pressures are greatest, and so pesticide residues are highest. By not considering the obvious seasonality of diet and residue levels, this CRA has underestimated risk. NRDC regards this omission as of great importance, and asks that that this be quantitatively considered in the CRA, either through the appropriate incorporation of seasonality data, or by use of safety/uncertainty factors.

III.F. The current CRA model does not account for the "left over" food, where elevated residues are consumed for an extended period of time

NRDC suggests that EPA attempt to better capture the "left over" food scenario, where a person purchases a contaminated food, and then eats that food for several meals. One reasonable approach to adjust for the fact that a person's eating habits, and associated residue exposure, is to hold the residue constant for the period that the "market basket" lasts – perhaps seven days. This "left over effect" captures the batch of groceries that may contain elevated residues, and are eaten for several days. This is not captured in the current CRA, and therefore the current assessment underestimates exposure. The rolling window approach suggested here allows a better alignment of the toxicology data with the exposure profile. The rolling averages presented by the Agency do not capture these real-world scenarios.

IV. INCORPORATE UNCERTAINTY INTO THE RISK ASSESSMENT

This preliminary CRA has numerous areas in which significant uncertainty arises, and these need to be acknowledged, quantitatively, by the Agency. As discussed in these comments, the preliminary CRA underestimates exposure in a number of key areas within the air, water, and residential risk components. In each of these areas, it is incumbent upon the Agency to adjust the overall estimation of exposure to adequately accommodate these uncertainties, and ensure that the final assessment will protect all fetuses, all infants, all children, and all adults.

V. VALIDATE THE RISK ASSESSMENT

It is good scientific practice to validate a model by comparing output results of several data sets within a single model, and between several models. No comparison was made between this model, Calendex™, which was designed and provided by Novigen, and other models. NRDC is very concerned about the use of the secret Calendex™ model, which is not available to outside scientists

for independent scrutiny. It was brought up by numerous members of the SAP, at several times throughout the three-day meeting, that any model, including the one used in this risk assessment, must always be tested with empirical data from real-world scenarios, when available. In addition, the assumptions and calculations underlying the model must be open and transparent to public and scientific scrutiny. A secret proprietary model is unacceptable as the sole source of data for the CRA. If this model is used it will be the Achilles heel of the entire risk assessment, since the assumptions hidden inside the 'black box' may drive the bulk of the results of the risk assessment. A public model must be used, and the Calendex™ model must be validated against other models and cannot be used alone.

In addition to public scrutiny and cross-validation of the models, NRDC encourages a comparison of the model output with existing monitoring and other real-world data, to "truth-test" the model. Data on organophosphate residues in human urine are being collected in numerous surveys, including the Agricultural Health Study, research conducted at the University of Washington by Dr. Richard Fenske and colleagues, and in the NHANES survey beginning in April 1999. In 1999, 703 people in twelve locations around the country underwent testing for six organophosphate pesticide residues in their urine as part of the latest NHANES. Residues tested included three ethyl organophosphate metabolites (diethylphosphate, diethylthiophosphate, diethyldithiophosphate) and three methyl organophosphate metabolites metabolites (dimethylphosphate, dimethylthiophosphate, dimethyldithiophosphate). At least eight pesticides in current use are metabolized into one or more of the ethyl organophosphate metabolites. Approximately eleven currently-used pesticides are metabolized into one or more methyl metabolites. It is possible to back-calculate from detected levels of the ethyl- or methyl-OP metabolites to potential levels of exposure. This calculation was illustrated by Fenske et al. (*32, 33*). Several assumptions would need to be made or modeled – including: (1) which ethyl or methyl pesticides the individuals sampled are most likely to have been exposed to, in which proportions, (2) whether all metabolites are present at the mean (or upper bound) concentrations found in urine, (3) what the total daily urine volume is likely to be, and (4) whether the concentration of pesticide in urine is assumed to remain the same throughout the day. Then it is a simple matter of performing a molar conversion to predict the likely exposures and compare these with the model and with the EPA reference doses for the individual pesticides. We strongly urge EPA to perform these calculations to truth test the model results and make sure that members of the population are not exposed to levels of OP pesticides that may pose a significant risk to health.

VI. CHARACTERIZE THE SHAPE OF THE DISTRIBUTION MORE ACCURATELY

When asked whether the SAP was comfortable with the presentation of data in the preliminary CRA as a uniform distribution, the answer was overwhelmingly "No". A uniform distribution presumes that all data, each value, has an equal probability of occurring. This is clearly not the case, Dr. Hattis (Clark Univ) pointed out. A uniform distribution will not capture the *not average* person, those people at the highest exposure level, and highest risk. Clearly, this is contrary to the FQPA, which demands that all people are protected. Dr. Adgate (Univ Minnesota) challenged the Agency to put some effort into characterizing the shape of the distribution, rather than presuming that a uniform distribution is a good fit of the data. Dr. Hattis said that it would be incorrect for the Agency to presume that the true high and low values can be determined from the small data sets used in this risk assessment. Dr. Freeman (Robert Wood Johnson School of Medicine, NJ) suggesting using medians, rather than means, if it better describes the data set. Dr. Hattis suggested that when the data sets are small, such as the case here, a lognormal distribution is usually the best fit. It was generally agreed by the SAP that any distribution that did not capture the tails, that is, those people who are most highly exposed, was unacceptable to the SAP.

NRDC suggests that the Agency make the necessary adjustments to the model distribution, according to the recommendations of the SAP as outlined above, such that all exposure scenarios, including those most highly exposed, are captured adequately. If this is not done, then the model will fail to fulfil the mission of the risk assessment, to assess the risk to the entire US population.

VII THE ROLLING WINDOW ARTIFICALLY DECREASES EXPOSURE, AND DOES NOT CAPTURE REAL-WORLD RISK

The concept of the "rolling window", as presented by the Agency, involves presenting the average for each 7-day, or 28-day time period. This results in a distribution of the weekly, or monthly, averages, rather than the daily exposures. The overall result is an artificial decrease in variability, decrease in exposure, and increase in MOE. This was pointed out by the SAP to be the likely result of a forced regression to the mean, and therefore not a likely representation of real-world risk. At the SAP meeting, Dr. MacDonald (McMaster Univ) pointed out to the Agency that a rolling averages model will reduce the extremes, and will therefore overlook real risk. Dr. Durkin supported this point, claiming that acute spikes would be obscured in such a model. NRDC agrees strongly with this point. Dr. Beth Doyle, EPA, presented pictorial representations of probability distributions, confirming that the rolling averages model would indeed obscure all peak data, thereby completely disregarding the data most of interest for risk assessment, and most of concern under FQPA. NRDC agrees with the SAP; this method will artificially lower exposure, while leaving tens of thousands of people at dangerous exposure levels, unprotected. This is scientifically untenable, and is in stark contrast to the spirit and the language of FQPA. NRDC recommends against using any rolling window time frame that effectively results in disregarding those individuals most at risk. The intent of FQPA is to protect all children, and not just those who are exposed to average amounts of toxic residues.

VIII. A NON-PROPRIETARY MODEL SHOULD BE USED ON ALL RISK ASSESSMENTS, NOW, AND IN THE FUTURE

Recognizing the uncertainty and potential for bias inherent in any model, NRDC requests that all assessments are done with the following safeguards:

1. Each risk assessment should be performed with two or more models, to begin to document model variability and model bias.
2. Each risk assessment should be performed using a non-proprietary model, in addition to any other models.
3. The need for uncertainty factors is required in calculating a margin of safety when a probabilistic risk assessment has been done.

The choice of an exposure model is an important one, as different models may use different assumptions about persons' activities and about the quantity of chemicals to which persons are exposed in varied environments. By accounting for input differently alternate models may produce dramatically different output estimates. Uncertainty arises in all model designs, because study conditions can vary dramatically from actual human environmental exposure. Risk assessments typically require scientists to extrapolate from experimental doses to environmental levels, from one exposure route to another (such as ingestion, inhalation, or dermal exposures), from one exposure pattern to another, and from small samples to large, more heterogeneous populations. Depending on the model chosen, these extrapolations may be made in different fashions, and one model may be much less health-protective than another. As EPA recently observed, "[t]he inherent uncertainty in models invites 'model shopping' and introduces too much uncertainty for use in risk assessments that support public health decisions." (Trichloroethylene Health Risk Assessment, April, 2001, Section 5.1) Therefore, NRDC makes the aforementioned requests.

IX. CONCLUSION

The Agency must recognize the many areas of the OP-CRA, which systematically underestimate exposure, or underestimate risk, many of which are discussed in detail in these comments. NRDC recommends strongly that the Agency incorporate these necessary changes, most of which were supported by the Scientific Advisory Panel. Without these corrections, the OP-CRA will not adequately protect the US population, and will therefore not legally meet the requirements of the FQPA. In this case, the Agency must acknowledge this shortfall, and apply uncertainty/safety factors sufficient to provide a margin of safety for the US population, including fetuses, infants, children, and the elderly.

Thank you for consideration of these comments,
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COVER STORY

Bad Science

EPA's industry critics urge Congress and the new administrator to upgrade the science used in regulatory decisionmaking. They are right that science at the agency needs improvement — largely because these same self-interested critics overwhelmingly dominate research agendas and peer review

LINDA GREER and RENA STEINZOR

"The right to search for truth implies also a duty: one must not conceal any part of what one has recognized to be true." —ALBERT EINSTEIN

In Washington circles, "sound science" has become the remedy of choice for most of what ails the regulatory system. Whether it's arsenic in drinking water or particulates in the air, proponents of this seemingly simple solution argue that if the Environmental Protection Agency would only get more scientists on board and listen carefully to their sage advice, we could eliminate or at least reduce those excessive health and safety regulations that squander public funds, freeing scarce resources to address far more urgent problems.

EPA indeed practices a great deal of "bad science," but not in the sense asserted by its industry critics. What really upsets regulated industry is not the agency's supposed failure to consider "good science." Instead, the business community is driven to distraction by the fact that EPA must make most decisions on the basis of incomplete or uncertain science. However, as we explain below, Congress and EPA administrators have long recognized that the agency must act in the face of uncertainty to achieve its mission. While it is important to debate the issue of how to operate in the face of scientific uncertainty, it is unhealthy to allow that debate to obscure far more profound and troubling problems with scientific practice at EPA.

Although agency scientists do many tasks, one of their most important responsibilities is to select the salient developments among various research methodologies and findings. It is critical that they perform this function with objectivity. If their analyses are infected with bias, their scientific practice, by definition, is unsound. Unfortunately, bias and secrecy increasingly compromise not only the work of EPA's in-house scientists, but also the ultimate failsafe intended to guarantee the soundness of agency science: peer review by the ostensibly independent and objective Science Advisory Board.

EPA science is dominated by self-interested industry research and peer reviewed by self-interested industry experts. The impact of these influences on the agency's rules is magnified by a lack of transparency about what pieces of research were used as the basis for important policy conclusions and why others were rejected. These problems are compounded by the fact that "science" at the agency is increasingly thrust into the role of final arbiter of all decisionmaking. Science cannot serve this purpose because the evidence on most issues considered by EPA is not definitive.

Two case studies support our diagnosis and suggest prescriptions for a cure. The first involves the inexplicable decision by EPA's Office of Research and Development (the primary location of in-house research and analysis) to revisit the toxicity profile of vinyl chloride and downgrade its estimate of the chemical's carcinogenic effects. The second involves a misguided opinion issued by the Science Advisory Board challenging an EPA staff conclusion that dioxin is significantly more toxic than first supposed. In both cases, experts working for chemical manufacturers dominated the process, managing to manipulate the pace, content, and final outcome of those deliberations.

At this point, readers may well wonder why, if the state of EPA science is as bad as we say it is, we don't agree with the critics who call for "sound science" — or "more science" or "better science, " etc. Many reputable people, including several generations of EPA administrators, have recommended the expansion and elevation of science within

the agency, arguing that it is the crucial, missing element of wise decisionmaking. In fact, this spring Congress may consider a bill by Representative Vernon Ehlers (R-Michigan) that would establish a deputy administrator for science, to centralize administration and evaluation of the agency's research. (See "A View from the Hill," page 30.) But, as we indicate at the top of this article, the call for sound science collapses two separate issues into one.

The first of these issues is the appropriate role of science in EPA decisionmaking: should scientific evidence serve as the sole determinant — or gate-keeper — of agency decisions whether to regulate? The second issue concerns the fundamentals of what *we* would call "sound" science: when EPA evaluates available technical information, what core principles must govern its deliberations to ensure scientifically valid results? An explication of where we stand on the first issue will make it clearer why we are so concerned about the second.

> ***EPA mismanages the scientific function to the point that it can no longer be relied upon to be either objective or fair***

The unavoidable reality is that, despite widespread demands that EPA employ more science, the scientific information available to the agency rarely gives definitive answers to the difficult questions that confront it. Toxicology, epidemiology, conservation biology, ecology — these and related fields have yet to produce research results that map a straightforward path to uncontroversial policy solutions. In many, if not most, cases EPA faces the conundrum of implementing environmental statutes that command it to protect public health and the environment from risks that are unknowable, understudied, or poorly understood from a scientific perspective.

Congress appreciated this problem when it passed the statutes that define EPA's mission. Look at the language of the basic laws that protect the air we breathe and the water we drink. The Clean Air Act commands the agency to protect public health with an "adequate margin of safety." The Safe Drinking Water Act requires the EPA administrator to regulate contaminants that "may have an adverse effect on the health of persons" where "there is a substantial likelihood" that the contaminant will be "of public concern" and present "a meaningful opportunity for health risk reduction." The Clean Water Act's central purpose is to "restore and maintain the chemical, physical, and biological integrity of the nation's waters," a phrase that has no defined meaning in science and requires human judgment.

As recently as last year, in *American Trucking Associations v. Whitman*, a unanimous decision authored by no less a regulatory skeptic than Justice Antonin Scalia, the Supreme Court reaffirmed Congress's Clean Air Act mandate that EPA protect public health with an adequate margin of safety and without regard to costs. Recognizing that this and similar mandates mean acting in the face of scientific uncertainty, Governor Christine Todd Whitman told the National Academy of Sciences in a speech delivered in 2000: "The absence of certainty is not an excuse to do nothing. . . . Environmental policy should always be based on the soundest information available at the time." The Earth Summit's action plan, Agenda 21, used similar language, admonishing all signatories (including the United States): "Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." Under all these formulations, the crucial challenge is to ensure that the available science is factually correct and appropriately interpreted, and is then weighed with other factors in making final decisions.

Consider EPA's efforts to reduce cancers caused by exposure to toxic chemicals. Despite decades of research, cancer remains a mysterious disease. Because we do not understand how it is triggered in the body, no scientist can tell how many people will suffer cancer following exposure to a given level of a suspected carcinogen. Given these and other gaps in our understanding of the toxi-

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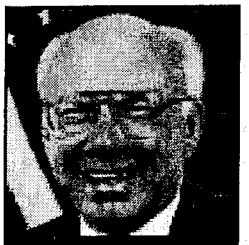
Both Sides Are Right: EPA Needs To Improve Science Function

The public discourse over how Environmental Protection Agency decisionmakers use science when determining controversial regulatory action or inaction always seems to fall into two camps. One view comes from the regulated community, who claim a controversial decision ignores the underlying science, which, in their view, shows the decision does more harm than good. Another view comes from environmental and public advocacy communities, who claim that the agency ignores the underlying science while letting the regulated community unduly influence the process. While these constituencies may forever diverge on the merits and effectiveness of a controversial decision, one theme is common to both camps — that science does not adequately imbue the regulatory decisionmaking process at the EPA.


Rep. Vernon Ehlers

The next stop for this debate is usually the halls of Congress and the judiciary, where these decisions are thoroughly scrutinized. Time and again I have heard my colleagues say, "What I really want is the use of sound science at the EPA." Time and again I have seen court decisions overturn a regulation because it did not have a proper scientific foundation. That science is not infused throughout EPA's regulatory process becomes a credible argument to wage both just and unjust legislative and legal battles over EPA action or inaction. Members of Congress and the judiciary do not have confidence that the agency uses science appropriately in its decisions. Science should not be used as a cudgel to win a battle, or as an afterthought to the regulatory process; rather it should serve as a decision's foundation.

Congressional and judicial doubt about EPA's process is borne out of both right and wrong motivations. However, it is not unfounded. Several independent reviews commissioned by Congress and EPA have concluded that there are significant problems with how science is used within the agency's decisionmaking structure. It is worth noting that these studies, for the most part, did not quarrel over the quality of the scientific research at EPA, but how it is used as proposed regulations move through the agency's bureaucracy.

In 2000, the National Academy of Sciences concluded a series of four reports collectively titled *Strengthening Science at the U.S. Environmental Protection Agency*. The NAS reviewed how science was conducted at EPA and incorporated into the regulatory decisionmaking process. The report concluded that while the use of sound science is one of the agency's avowed major goals, both intramural and extramural science should be more fully integrated into its management and decisionmaking structure.

The NAS concluded with this important statement: "The importance of science in EPA decisionmaking process should be no less than that afforded to legal considerations. Just as the advice of the agency's general counsel is relied upon by the administrator to determine whether a proposed action is legal, an appropriately qualified and adequately empowered scientific official is needed to attest to the administrator and the nation that the proposed action is scientific."

In a 1998 science policy report, approved by the House Science Committee and the full House, titled *Unlocking our Future: Toward a New National Science Policy Study*, I had reached similar conclusions about the use of science in decisionmaking — that science should not be used as a mere adjunct to the regulatory system; rather, it should be used at the beginning, middle, and end of an agency's decisionmaking process — and about its proper place in an agency's bureaucracy.

I introduced H.R. 64, The Strengthening Science at the Environmental Protection Agency Act, to capture the two primary recommendations of the NAS report and meet the goal I laid out in the science policy report. First, the legislation would establish a new Deputy Administrator for Science and Technology to serve as an advocate for and reviewer of science at the most senior levels of the agency. Second, the legislation would convert the position of the Assistant Administrator of the Office of Research and Development to a set term and give that position the title of the agency's Chief Scientist.

The Deputy Administrator position will bring a much needed change to the culture of the EPA and ensure that science has a higher profile in the agency's decisionmaking process. This person would not only be accountable to the administrator for improving and overseeing science at the agency, but would also be accountable to Congress. This relationship would bolster Congress's confidence in the appropriate role of science at EPA, and therefore in regulatory decisions.

The Deputy Administrator is also needed to coordinate research between the regulatory and scientific arms of the agency. A common problem with trying to ensure that science is involved throughout the regulatory process is that the head of the scientific arm of the agency, the Assistant Administrator for ORD, shares the same rank as the heads of the regulatory offices. The authors of the NAS report argued that since the new Deputy would rank higher than the existing AAs, this person could foster research relationships between ORD and the regulatory offices.

Furthermore, the Deputy Administrator could develop and oversee an agency-wide inventory of scientific activities. Various efforts to do this inventory have all died after fits and starts because there is no central science policy authority to administer this work. The Deputy Administrator would have the appropriate authority to ensure that the best possible peer-review and research-plan-

ning practices are used for all of the agency's scientific endeavors.

While the first recommendation of the legislation and the academy report is intended to increase the political clout that science has at the agency, the second recommendation, to establish a set term for the AA of ORD, seeks to decrease political pressures on this office. The report notes, "Although the political aspect of the Assistant Administrator's job often receives considerable attention, the most important aspects of the job are not political." Since the Deputy Administrator could bear many of the political pressures inside the agency, the AA for ORD could refocus on his or her role as the agency's Chief Scientist and running a world-class scientific organization.

The tenure of an AA for ORD averages two to three years and is typically a lower priority appointment in new administrations. Under the current political appointment model, this position changes at least as often as the administration changes. The NAS noted that frequently changing goals, priorities, practices, structure, or funding are particularly disruptive to research organizations because of the long-term nature of research activities. Research endeavors cannot be easily stopped and then started again without significantly hurting productivity. A longer tenure for the AA would help insulate the office during changes in the administration, thereby providing more continuity for research conducted at the agency.

The NAS report captured the challenge that EPA's science mission faces in the future and the need to strengthen science at the agency by saying, "In the three decades since the U.S. Environmental Protection Agency was created, great progress has been achieved in cleaning the nation's worst and most obvious environmental pollution problems. Belching smokestacks and raw-sewage discharges are now scarce, and air pollution alerts and beach closings are more rare. EPA deserves a significant share of the credit for the accomplishments, but some of the most difficult and challenging tasks remain. Many past illusions about simple and easy solutions to environmental problems have been replaced by greater realization that environmental protection is a complicated and challenging mission." It is time that Congress and EPA rise up to meet this challenge by passing and implementing the provisions of H.R. 64.

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cology of common chemicals, EPA must act in advance of definitive scientific evidence in order to fulfill its statutory mandate to protect human health. If scientific evidence is called upon to resolve policy disputes where definitive answers are unavailable, science will lose the unique value it has to policymakers, converting the interpretations of scientific findings into an exercise in advocacy rather than an ongoing quest for truth.

Since such a broad and authoritative range of policymakers, over the course of several decades, have recognized that scientific uncertainty is inevitable, why is it so difficult to resolve the equally inevitable question of how much uncertainty is too much? Recent developments suggest that regulated industries use routine scientific data gaps opportunistically, by insisting that until EPA has "better science," it should not act. The infamous case of how much arsenic should be allowed in drinking water illustrates this phenomenon perfectly. In 1996, a unanimous Congress told EPA to change the 50-year-old standard that scientists conceded was not adequate to protect public health. The agency's in-house scientists worked diligently over a period of several years, supplemented with expert panels convened by the National Academy of Sciences. EPA conducted an exhaustive rulemaking that gave affected constituencies ample time to submit information. Cumulatively, the research demonstrated that EPA should lower the standard dramatically to avoid unacceptable adverse health effects, although the scientists could not reach a consensus on the appropriate numerical level. As is usually the case, there was no science that indicated precisely when exposure levels stop being "safe."

Operating competently in the face of remaining uncertainties, EPA Administrator Carol Browner was close to making a new standard final late in the Clinton administration when congressional appropriators invoked the specter of incomplete — and therefore "bad" — science in order to delay promulgation of the rule into the new administration. Browner nonetheless published the standard as final right before George W. Bush took office as president. Then, as the appropriators and their allies, mining interests and drinking water system operators in the West, had hoped, Whitman moved to delay the rule's effective date, declaring that she wanted to review the adequacy of the underlying science. Subsequently confronted

with consistent support from NAS experts for an even tougher standard, Whitman ultimately was forced to reverse her decision and allow the promulgated standard to go into effect. The arsenic episode is a powerful example of how, even when the National Academy of Sciences concludes that there is sufficient basis to lower allowed exposures to a toxic chemical, enough is never enough for those whose true intent is to hold back government intervention to protect public health.

Scientists are comfortable with data gaps and uncertainties. They view them not as "problems" but as future research agendas. It is policymakers who are plagued by these realities because they must make decisions in the face of uncertainty or stop trying to protect public health until some indefinite, far-off day. As the arsenic example reveals, the call for "more science" heard in the halls of Congress and from regulated industries often serves as nothing more than a ruse for indefinite delay on a rule, sometimes for decades. Given the political muscle of those who have mounted this campaign, scientists watching these developments from the sidelines would do well to take note: the fruitless quests for more and more definitive evidence from environmental policymakers unwilling to suffer political consequences for restricting pollution will inevitably make scientists the whipping boys for the consequences of regulatory gridlock. Unless we recognize that "science" cannot determine all that EPA is required by law to do, the agency will never have the breathing room it needs to craft wise policy.

As important as the issue of what role science can and should play at EPA is the issue of the fundamental principles that should govern the agency's on-going scientific deliberations. In this long-overlooked area, we have found problems that would shock most traditional, academic scientists. The remainder of this article is devoted to demonstrating our case that too much of the science used by EPA is intrinsically unsound, straying far from the principles that have long served as the ground rules of the discipline. Too often, EPA deems scientific evidence supporting more rigorous standards to be marginal and more readily accepts research suggesting that standards can be loosened. We begin with a review of the principles that define *truly* sound science and then apply those standards to the recent vinyl chloride and dioxin reassessments.

Congress and EPA administrators have long recognized that, as required by its core statutes, the agency must act in the face of uncertainty to achieve its mission

Science enjoys a unique reputation as an objective and dispassionate human endeavor. Because we consider it to be inherently unbiased, science is accorded a privileged role in deliberations about the organization of human affairs. Unlike many other human endeavors, scientists preserve the integrity of the scientific process exclusively through self-regulation. Although there are isolated examples of outside, lay investigations challenging the credibility of scientific research, the repetition of experiments by fellow scientists and objective peer review are the routine methods for uncovering mistakes and assessing when progress in understanding a topic has been made.

For centuries, scientists have engaged in their search for the truth by circulating the results of original research among their colleagues, first for informal discussion and then for formal, outside peer review. Colleagues first repeat work accomplished by others and then extend the experiments into additional areas. By exposing all of the underlying elements of one's work to inspection by dispassionate peers, and revealing details sufficient to replicate results, researchers build on others' successes and avoid others' failures.

The transparency of results and the impartiality of conclusions derived from those results are the indispensable foundation of science. Peer review and replication are the only reliable methods to ensure that experiments are conducted in a scientifically appropriate manner and that the results and conclusions presented by the researchers are supportable by the data generated. The peer-

review process is often challenging and difficult. But without it, results and conclusions cannot be accepted as valid.

The public trust in science depends on its unique reputation for objectivity. Scientists are expected to have opinions, but are also expected to resist bias. They are expected to reach careful conclusions and limit their conclusions to those supported by data. Or, to put this central principle more crassly, a scientist's quest for the truth and expression of opinion at the end of the quest should not be for sale or subject to control by self-interested sponsors, supervisors, the government, or any other entity with control over the scientist's career. Once financial considerations and legal constraints interfere with a quest for scientific truth, the public trust is broken, and science loses its power and authority.

Unfortunately, funding for the replication of experimental results and peer review of scientific research is most abundant in the context of topics that have captured public attention or, to put it another way, where the results of the research are of widespread economic or social importance. Claims that a scientific team had created cold fusion were immediately dissected because of the potentially monumental implications of such a discovery on the world's need for safer and cheaper energy. Similarly, discovery of a wonder drug to treat such widespread ailments as diabetes or stroke would inspire careful and extensive inspection — by the discoverer's competitors, potential allies, the larger medical community, and the government.

If scientific evidence is called upon to resolve policy disputes where definitive answers are unavailable, science will lose the unique value it has to policymakers

In a modern world overwhelmed by information and disinformation, extensive peer review or replication of certain other types of scientific findings is difficult to instigate, especially in the private sector. So, for example, efforts by a chemical manufacturer to prove that a given substance is not as toxic as EPA had originally assumed are unlikely to be scrutinized, much less validated, by other private sector scientists. Competitors have a low interest in refuting such results because they typically manufacture the same chemical and like the way the results came out. Only producers of an arguably safer alternative have an economic incentive to second-guess, and they would likely place a higher priority on testing their own compounds.

For better or worse, these economic incentives mean that the government must play an active, rigorous role in reviewing and challenging scientific research developed by self-interested private parties. The National Academy of Sciences, the National Institutes of Health, and the Centers for Disease Control, to name just a few, have erected infrastructures of in-house scientists and external peer-review panels to undertake these functions. Unfortunately, these outside institutions have limited resources and too rarely are able to double check EPA's work.

Science at EPA supports decisionmaking through two main activities. In-house scientists assigned to the Office of Research and Development analyze the outside studies that are relevant to the issues at stake. They maintain the Integrated Risk Information System, or IRIS, an internationally influential compendium of "toxicological profiles" that describe the characteristics of specific chemicals and set quantitative levels for safe exposures to them. Our case studies involve reassessments of long-standing toxicological profiles. The second activity is peer review, performed by panels of outside experts convened by the EPA Science Advisory Board and several other, smaller boards, such as the Science Advisory Panel, which focuses on pesticides. The SAB receives inquiries from agency staff working on regulatory issues and responds with advice based on its assessments of relevant scientific research. Our dioxin case study concerns an SAB peer review.

Many of EPA's in-house scientists and SAB experts serve the agency and the public with distinction, laboring diligently to produce informative and dispassionate science to guide policymaking. Too often, however,

both enterprises flout the fundamental precepts of scientific research: first, the disclosure of methods, data, and calculations sufficient for appropriate experts to review the work or evaluate whether the conclusions reached were adequately supported by the study's findings and, second, conducting peer-review that is free of conflicts of interest.

Even a cursory look at the science EPA has practiced over the past decade shows that it has strayed far from the mandates of transparency and impartiality. Much of the science that EPA uses as a basis for decisions with far-reaching implications for public health is not peer-reviewed, and it is often based on confidential information or analysis. As a result, it would not be considered credible by disinterested researchers.

At the root of this crisis in credibility is the dominance of industry funding as the source of support for environmental health research. The vast majority of research on the toxicological properties of common chemicals occurs outside of the government (or sometimes in other agencies). EPA's toxicological profiles are based on this outside work. Corporate sponsorship does not, in and of itself, render such research invalid. But it does unquestionably put industry in the driver's seat for both the pace and focus of data development to support EPA rulemaking. More insidiously, it also puts industry in charge of deciding what information it would like to disclose and what analyses it would like to do, presenting ample opportunities for industry-funded researchers to keep underlying data and discrepancies confidential and to make strategic decisions as to whether to submit research studies for EPA's consideration.

Vinyl chloride is notorious for causing liver cancer among workers handling it. Studies have also linked vinyl chloride to a number of other cancers, including brain cancer

For several decades, the scientific community has achieved a rare consensus that three substances — lead, asbestos, and vinyl chloride — are not just extraordinarily toxic but produce well-characterized consequences of exposure, known colloquially as "fingerprint diseases." Vinyl chloride, a volatile industrial chemical used since the 1930s to make plastics, is notorious for causing a rare and serious tumor, angiosarcoma of the liver, primarily among workers manufacturing and handling the compound. Studies have also linked vinyl chloride to a number of other cancers, including brain cancer.

In 1975, following a series of animal and epidemiological studies demonstrating the chemical's hazards, the Occupational Safety and Health Administration used the evidence on liver cancer as the basis for tough regulations limiting workplace exposure. These regulations resulted in sharp reductions in the prevalence of the chemical in the workplace and, as a result, the environment.

So it was a surprise when, in May 2000, EPA completed a 20-fold downgrading of the toxicological profile for vinyl chloride. EPA's decision to review vinyl chloride's toxicity was especially startling because the OSHA regulations, among other factors, have had their desired effect. At the same time that worker exposures have plummeted in the last decade and public exposure to the chemical has been minimal, industry has been able to continue using it, producing such goods as upholstery and waterpipes from its polymerized form. Given the demonstrated benefits of the regulations to both workers and industry, and the greatly lowered risk to the public, vinyl chloride should be off the list of chemicals requiring toxicological review, leaving the agency free to pursue more prevalent, less understood chemicals.

The decision to revisit the well-trodden ground of vinyl chloride toxicity appears especially irrational because EPA has faced extensive criticism for failing to assess the toxicity of many other chemicals produced and used in large amounts annually. EPA has *no* toxicity information on 43 percent of the nearly 3,000 organic chemicals produced or imported in amounts above one million pounds annually, and a full set of basic toxicity information is available for only 7 percent. Toxicological studies of these chemicals should be its overriding priority.

Further, little new technical information on vinyl chloride's toxicity has become available since the agency's last review of the chemical, in 1994. Instead, EPA staff based the reassessment on animal studies completed in 1991 and earlier. Only one unpublished epidemiological study update was new, and it reached conclusions similar to previous analyses.

Although no changes in existing regulations were made when EPA made its decision, the revised characterization of the hazards posed by vinyl chloride exposure will prove very valuable to manufacturers of the chemical now engaged in toxic tort litigation with workers who contracted brain cancer following exposure on the job, as well as companies still facing liability at Superfund sites contaminated by the chemical. (Vinyl chloride has been found at one-third of the sites on the National Priorities List.) The decision will have these effects because EPA's toxicological profiles play the crucial role of informing regulatory and judicial decisions — not just domestically but internationally. Regretfully, given the potential implications of this change, the details of EPA's reevaluation of the science reveal biased technical judgment that resulted in poor selection of evidence practices and disproportionate reliance on information generated by self-interested parties.

OSHA regulation of vinyl chloride has worked. So it was a surprise when, in May 2000, EPA completed a 20-fold downgrading of the chemical's toxicological profile

EPA made two fundamentally flawed decisions in justifying the downgrade. First, the agency decided to confine its reassessment to statistically significant liver tumors, ignoring the various other cancers that frequently appear in both animal and epidemiological reports. Second, although the reassessment continued to rely on animal data, EPA decided to abandon certain default "safety factors" it has historically used when applying animal data to humans. Instead, the agency relied on a newly developed, "pharmacokinetic" model designed to predict an internal concentration of vinyl chloride in the human body.

Epidemiological studies of vinyl chloride workers have generally reported the occurrence of many cancers besides liver angiosarcomas, including cancer in the lung, lymphatic and blood tissue, and the brain, with the last of particular concern. Richard Monson first found an excess of brain cancers in his study of Swedish workers in 1974, as did Irving Tabershaw and William Gaffey in 1974 and Richard Waxweiler in 1976. In 1981, W. Clark Cooper enlarged the Tabershaw and Gaffey study and found statistically significant increases in brain and central nervous system malignancies. In a 1991 update of the Cooper study, Otto Wong confirmed statistically significant brain cancers. The evidence concerning brain cancers is sufficiently convincing that in 1989 the Vinyl Institute, an industry-funded advocacy group, acknowledged brain tumors as a valid concern in a letter to the California Air Resources Board: "For brain cancer, three out of five studies demonstrate statistically significant findings, although the results were somewhat variable. Positive findings occurred in studies with the greatest statistical power."

Written correspondence included in the EPA docket on vinyl chloride reveals that the Chemical Manufacturers Association, the trade association that recently was renamed the American Chemistry Council, became quite upset with Wong for publishing his positive results on brain tumors without first submitting the study to its scientists for review. Wong did the work under a research contract with CMA that apparently included a "prior review" clause giving it the right to comment before publication.

In what was likely a response to the trouble that the Wong update caused industrial users of vinyl chloride, CMA commissioned yet another study of the same worker cohort, updating some data post-Wong but also re-analyzing some of Wong's data in a way that raised questions about his conclusions. This study was never published in a peer-reviewed journal, but it was submitted to EPA

and became a primary basis for its 2000 reassessment.

In justifying its decision to focus exclusively on liver cancer in recalculating the vinyl chloride potency factor, EPA cites this unpublished work, as well as two peer-reviewed research review articles. The unpublished CMA study was not, by itself, a sufficient basis for EPA to eliminate brain cancers from its list of concerns. To the contrary, this study also reported statistically significant incidences of brain cancers.

As for the two articles reviewing available research (as opposed to reporting the results of original research), the first was written by Sir Richard Doll in 1988, two years before the publication of the Wong study. Without the benefit of the Wong or subsequent epidemiological updates of vinyl chloride workers, Doll had raised questions about the strength of the data supporting brain tumors, but had concluded with the relatively mild statement: "There is too little evidence either to confirm or refute the suggestion that vinyl chloride might cause melanoma or cancers of the thyroid, brain, and lymphatic and hematopoietic systems." This equivocal conclusion from an outdated paper hardly provided a reliable basis for ignoring the numerous studies in EPA's decisionmaking docket that found statistically significant incidences of brain tumors. Indeed, Doll has cautioned against using epidemiological results to dismiss chemical hazards in this and other publications.

The other cited research review article was authored by Jan Storm and Karl Rozman in 1997, but it does not address the issue of brain or other tumors caused by vinyl chloride exposure. Rather, the paper compares various risk assessment extrapolation models used and proposed by EPA. Given the weakness of Doll's conclusion, and the inappropriateness of the Storm and Rozman citation, EPA is left without evidence to support its decision to limit its reassessment of vinyl chloride's carcinogenicity only to tumors of the liver.

In justifying its downgrade of vinyl chloride, EPA cites an unpublished, review and two reviews of technical literature, one outdated, the other irrelevant

EPA's second technical misstep was the decision to abandon the conventional approach used to apply animal data to likely human health effects. When scientists conduct animal studies, they expose the animals to increasing doses of a chemical, and then perform an autopsy on the animal to see how many tumors were generated at each dose. Because chemicals may take a different course within the bodies of rats, mice, and other creatures than they do in the human body, and may be metabolized at different rates, animal studies using traditional dose measurements can either overstate or understate the consequences of comparable human exposures. Up until recently, the best way to eliminate such uncertainties would be — hypothetically, that is — to intentionally expose people to different amounts of a chemical and then track the "fate and transport" of the chemicals within their bodies by drawing samples, taking biopsies of organs, etc. Such studies should be unthinkable for obvious reasons.

Pharmacokinetic models are an emerging, as yet experimental, alternative method designed to bridge this gap. Such models estimate internal concentrations within the human body by using a computer program to predict how fast the chemical is absorbed in the bloodstream, whether it reaches the brain, etc. The models then derive an "effective" dose for a given organ over the time that the human body metabolizes the chemical. If doses of vinyl chloride at X levels caused Y incidences of tumors in rats, but pharmacokinetic models show that humans metabolize the chemical more effectively than rats, and therefore experience lower internal concentrations, the model provides support for downgrading estimates of the chemical's carcinogenic effects on people.

The catch here is that pharmacokinetic models are at the cutting edge of the already highly uncertain science of environmental modeling as a whole. It is certainly true that reputable scientists are working to refine

such models in order to better predict effects of exposure. It is also likely that, once they are developed, such models should allow us to better understand the correlation between internal concentrations of toxic compounds and adverse health effects. But at this point in the evolution of scientific understanding, these models cannot be validated with respect to exposures at environmentally realistic concentrations. This uncertainty means that pharmacokinetic modeling unquestionably does not put EPA in a position to remove default safety factors.

Mindful of these concerns, when EPA staff considered the application of pharmacokinetic models in a proposed reassessment of the toxicological profile of trichloroethylene, they made a concerted effort to compare several versions of the models, as well as to quantify the level of uncertainties in each model's estimates of liver, lung, and kidney tumors in response to the modeled doses. This analysis quantified uncertainties so huge (as high as 20,000-fold) that EPA staff insisted on continuing to apply default safety factors, thereby sharply curtailing their reliance on any of the models. This carefully qualified application of an emerging scientific methodology stands in stark contrast to the wholesale reliance on pharmacokinetic modeling results in the context of the vinyl chloride reassessment. Such extraordinarily high rates of uncertainty raises obvious concerns about modeling accuracy, as well as concerns about "model shopping" by researchers trying to find a model that gives a desired outcome rather than one that predicts outcomes accurately.

The agency removed default safety factors in applying animal data by relying on an unproven computer program designed to model how a chemical behaves in the human body

The general problems of pharmacokinetic models are severely compounded in the case of vinyl chloride by EPA's decision to confine its consideration of modeling to a single version developed by Harvey J. Clewell. The Clewell model was not validated for exposures that occur routinely in the environment. It thus could not and was not validated for its intended purpose — to accurately predict effects in humans. The inadequate verification of the Clewell model makes it a very poor policy choice as a basis for the reevaluation of vinyl chloride toxicity. Furthermore, the Clewell model was confined to liver tumors, ignoring all the other tumors of concern. Using such a limited model to justify dropping safety factors for cancers other than liver cancer added insult to injury.

The fatal blow to the technical credibility of EPA's vinyl chloride decision is that industry scientists drafted the final decision-making document. The revised toxicological profile, known formally as the 2001 Vinyl Chloride Toxicological Review, is known in the world of science as a "technical review paper," consisting of a literature collection, analysis, and interpretation. Vinyl chloride is but the first of four chemicals where industry is drafting the review. (The others are styrene, ethylene oxide, and toxaphene.)

In the scientific community, it is widely understood that technical reviews, like similar efforts in other disciplines, are heavily influenced by an author's subjective judgment regarding such issues as which studies to include, which studies to declare flawed or irrelevant, and which methodologies to favor. The danger of tainting a technical review with the unrestrained bias of its author provoked the prestigious *New England Journal of Medicine* to prohibit "editorialists and authors of review articles" from having "*any* financial connection with a company that benefits" from the subject of the article. The *Journal's* decision was announced in a lengthy editorial published in 1996 expressing mortification about its earlier publication of such a paper authored by two industry experts with obvious, but undisclosed, conflicts of interest.

In theory, EPA's Science Advisory Board is where the buck stops on bad scientific practice within the agency, serving as a safety net to protect against the types of abuses that run rampant when the generation of scientific evidence and the

selection of salient research are both determined by industry. In reality, the SAB suffers from many of the same weaknesses that were manifest at the staff level in the vinyl chloride reassessment. Too often, the SAB operates in a context where self-interested research dominates the agenda of the outside experts recruited for peer review. The seriousness of these problems is exacerbated when studies important to EPA, such as those specifically delineating the potency of a certain carcinogen, have not been published in a peer-reviewed journal and therefore were never subject to an objective evaluation by a disinterested party.

Last June, a General Accounting Office report evaluating the SAB review process found that "to be effective, peer-review panels must be . . . free of any significant conflict of interest and uncompromised by bias." In the report, "EPA's Science Advisory Panels: Improved Policies and Procedures Needed to Ensure Independence and Balance," GAO auditors examined the procedures employed by SAB staff to ensure panel effectiveness. GAO found that, despite the requirements of the Federal Advisory Committee Act, agency staff often failed to obtain conflict of interest disclosures from candidates and that EPA did not have either the information or processes in place that would preclude the appointment of panelists with direct conflicts of interest. The result of these omissions is the appointment of too many panels disproportionately influenced by industry experts motivated to clear chemicals of prior findings of toxicity. Many SAB panels escape this fate, but enough suffer from these ethical lapses to undermine the credibility of the entire EPA peer-review process.

One example of these problems is EPA's star-crossed effort to strengthen public health standards for arsenic in drinking water, mentioned earlier. An SAB review panel took on no less an entity than the NAS arsenic panel. NAS experts typically spend two or more years reviewing available science on an issue, and this particular panel had clearly mastered the data before it recommended tightening the standard. In contrast, SAB panels too often make recommendations within a period of a few months and with many fewer world-renowned experts. Only after an additional NAS panel took the SAB panelists to task for flaws in its analysis did the SAB panel back off its contention that EPA's in-house scientists had erred. Although this episode had a happy ending, the SAB arsenic toxicity panel was part of the problem, not the solution, of this contentious public health debate.

After a decade of research pursuing claims that dioxin is not as toxic as initially thought, agency staff concluded that the chemical is in fact more toxic than original estimates

But perhaps the best case study of the weaknesses that increasingly overwhelm the SAB is its participation in the reassessment of dioxin, which is released by incineration of chlorinated materials and also by paper bleaching. Starting in 1990, EPA staff spent a decade pursuing claims that dioxin was not as toxic as initially thought, producing a final report consisting of several thousand pages that concluded the opposite: that dioxin is even more toxic than the agency's original estimates. But an SAB panel appointed to peer review a draft of the study concluded in 2001 that in-house scientists had exaggerated the risks posed by exposure to the chemical. These assertions not only challenged the competence of the EPA staff who wrote the report, they erected a barrier to its release. During the public outcry that followed, it emerged that a large number of panel members had worked for — or received funding from — industries with a clear financial stake in the outcome of the deliberations.

For example, John Graham, a political scientist appointed to the panel, served as director of the Harvard Center of Risk Analysis, which receives extensive funding from companies facing liability for dioxin contamination of the environment. (Graham now serves as head of the White House's Office of Information and Regulatory Affairs, which evaluates the

costs and benefits of rules before they are published as final. The Natural Resources Defense Council opposed his nomination.) Appointment of a second panelist, Dennis Paustenbach, was questioned for similar reasons. Research by the Center for Health and Environmental Justice found that fully a third of the panel members received organizational support from 91 dioxin-producing companies. As a result, members of Congress accused EPA of setting up a panel dominated by industry bias. Witnesses at the public hearing on the results of the SAB peer review repeated these charges, questioning the credibility and the integrity of the panel.

Yet the clear appearance — and likely existence — of impropriety is only a threshold conclusion that should prompt further investigation. Regardless of the panelists' links to self-interested industries, the crucial point is the soundness of the SAB's assertion that EPA staff did not consider alternative scientific theories about dioxin's toxicity and, as a result, overstated the degree of scientific certainty regarding the overall toxicity of the compound. Stung by these attacks, William Farland, the acting deputy assistant administration in charge of the reassessment, took the unusual step of entering the fray. In defending the agency's work, Farland provided the SAB's Executive Committee, which must ratify all SAB panel reports, with nine pages of blistering comments on the panel's draft. He said that the review contained "numerous errors or distortions of fact" and that its major conclusions "defied logic." He added that the panel's report was internally inconsistent with the discussion of the science held in open session at prior review meetings; was inconsistent with advice provided by SAB panels on earlier versions of the reassessment; and was inconsistent with EPA's general risk assessment procedures.

Farland was particularly critical of the SAB's review of the dioxin risk assessment methodology, asserting that the panel had a poor understanding of both EPA guidance on risk assessment and the research available on dioxin. For example, the panel had questioned whether a "linear dose response curve" for cancer was warranted because there is some evidence that dioxin is a promoter of the disease, rather than an initiator. A linear dose response curve is a line that runs all the way down to a dose of zero. It is used when evidence is inconclusive as to whether there is a threshold dose below which exposure does not cause cancer. In the interest of safety, where data are inconclusive, a linear curve assumes that any dose — no matter how small — will lead to an adverse health effect.

The SAB attacked the staff report. It said that dioxin does not initiate cancer but promotes existing cancers. And it said that low doses of dioxin might actually be beneficial

The SAB panel argued that exposure to dioxin exacerbates the growth of cancerous cells that have already begun to grow in the body as a result of another cause, but does not itself initiate the cancer. In other words, there is a threshold, the panel said, below which dioxin exposure is unimportant because some other factor is causing the disease. The panel further complained that use of a nonlinear model would have resulted in a significant downgrade of the chemical's overall toxicological profile because it would have shown that small doses of the chemical are not harmful. "Belief is one thing," Farland responded, "data is another." EPA policy commands the use of a linear model when use of alternative models cannot be justified from the available data, as was the case here. There were neither data nor policy justifications to diverge from a linear default model for dioxin's cancer effects.

Similarly, Farland was incredulous that the SAB panel gave credence to the possibility that very low doses of dioxin were actually beneficial, resulting in decreases in cancer rates. The panel had urged EPA to give this counter-intuitive possibility additional scrutiny. However, EPA's extensive data showed that dioxin could cause adverse health effects at the relatively low levels that already occur in the general population. Farland pointed out that animal data are unequivocal on this point and that human data, though limited, are also compelling.

Ultimately, the controversy triggered by the panel's report on dioxin compelled the SAB Executive Committee to substantially rewrite the summary and conclusions of the report, producing a credible outcome — but illustrating the perils of lax ethical rules in lower-profile proceedings. Recognizing that this incident and the GAO report threatened the credibility of the SAB itself, the Executive Committee agreed to set up a subcommittee that will recommend reform of SAB policies and procedures on bias and conflict of interest.

As it crafts these policy and procedural guidelines for release later this year, the SAB will undoubtedly consider the approach taken by 12 medical journals that have faced equally serious challenges to their reputations as sources of credible life science in the context of pharmacology, a discipline that is the genesis of environmental toxicology. The crisis in the medical community started simmering in 1988 when the Boots Company, a British pharmaceutical manufacturer, hired Betty Dong, a researcher at the University of California in San Francisco, to do a research study designed to demonstrate the superiority of the company's bestselling thyroid medication, Synthroid, in comparison to generic versions. With Synthroid sales in the $600 million range in the United States alone, Boots had a large stake in demonstrating that generic versions are not "bioequivalent," and therefore should not be substituted for its name brand. To Boots's horror, the study found that the generics were in fact bioequivalent. The company then spent four years working to discredit the research, raising a litany of technical objections to its protocols and their implementation. Despite this campaign, extensive investigation upheld the soundness of the study.

In 1994, in the midst of this maneuvering, Dong submitted an article based on the study to the *New England Journal of Medicine*. The article, accepted for publication following peer review by five outside experts, explained that the finding of bioequivalence meant U.S. health care costs could be cut by $356 million annually if patients substituted generic medications. The company immediately threatened to sue Dong, citing a provision in her research contract that required her to obtain the company's written consent before publishing. The University of California began to waver in its support, and Dong pulled the piece, triggering an intense investigation by the publication.

The *Journal* finally published the article in 1997, along with an article reporting that in a survey of 2,100 life science researchers, nearly 20 percent reported having delayed the publication of research results for more than six months. Of the 410 researchers willing to report such delays, 28 percent said the reason was "to slow dissemination of undesired results." A subsequent Carnegie Mellon University canvass of contracts at university-sponsored research centers found that 35 percent of signed agreements allowed sponsors the right to delete information from publication; 53 percent allowed publication to be delayed; and 30 percent allowed both. To medical journal editors, these troubling findings were the unavoidable byproduct of sharp increases in industry funding and increased blending of business interests and science at both the individual researcher and university levels.

The agency must reserve for its staff the sensitive task of writing toxicological profiles and should never again delegate such work to self-interested industry scientists

What are the implications of this all-pervasive industry funding of university research? In a recent article published in *Risk Policy Report*, David Clarke, a longtime observer of the controversies involved in toxic regulation who now participates in the sound science debate on behalf of the American Chemistry Council, argued that the simple fact that a study is funded by industry does not mean that it is wrong, or even biased. Regardless of whether you accept this counter-intuitive argument that money does

not buy influence, it is certainly true that industry-sponsored research will remain the primary source of information on toxics for the foreseeable future and that effective reform must be premised on that fact.

Empirical studies have documented the correlation between funding and results. For instance, one analysis found that 98 percent of industry-funded research reported positively on the efficacy of specific drugs, versus 79 percent of independent research. Because we cannot eliminate our dependence on such research, but suspect that funding may affect the outcome, all the other checks and balances — from disclosure of funding sources to peer review — become all the more important.

Last September, in reaction to stories and statistics like these, the editors of the world's leading medical journals announced that they would no longer "review or publish articles based on studies that are conducted under conditions that allow the sponsor to have sole control of the data or to withhold publication." The editors promised to release detailed guidelines on this prohibition, and on their intention to require authors to disclose conflicts of interest related to a study, in early 2002. "I am not against pharmaceutical companies," Catherine DeAngelis, editor of the *Journal of the American Medical Association,* told the *Washington Post.* "What I object to is the use of my journal as an advertisement mechanism rather than a vehicle for the distribution of sound medical science."

The journals' new policy is expected to have a profound effect on the way medical research is funded and conducted. The journals are crucial to the dissemination of pharmaceutical research among the practicing physicians who serve as purchasing agents for all prescription drug sales. Television and print advertising are poor seconds to the influence they wield. Although these same reforms are necessary in the arena of environmental research, they may prove much harder to accomplish, especially given the fundamentally different economic incentives at work in investigations of the toxicological properties of common chemicals. In too many cases, chemical manufacturers have powerful incentives *not* to know whether their products are toxic; ignorance may help them sidestep liability and increased regulation. Unlike medicine, where publicizing efficacy is the quid pro quo for selling drugs, documenting the possible consequences of chemical exposure can only have a negative impact on sales. In fact, the only kind of scientific inquiry with potentially substantial financial benefits is research that exonerates chemicals — such as the two examples featured in our case studies.

EPA should establish a peer review process that eliminates panelists with actual or potential conflicts of interest and balances competing scientific views

As Wong's experience with the American Chemistry Council shows, the corporate funders of investigations into chemical toxicity, like the pharmaceutical companies, impose restrictive arrangements on their grantees. Given the dearth of government funding for such basic research, and the fact that it is unlikely to bring prestige to any truly independent research institution, these restrictions are likely to persist in the absence of strong action by EPA and other regulatory agencies.

Six categories of reform are needed to restore the credibility of science at EPA. First, the agency must focus on encouraging research that will close the gap in our understanding of the toxicity of common chemicals, rather than spending scarce resources on efforts to exonerate chemicals with a proven track record. Second, EPA must refuse to consider, in any context, the results of research that does not satisfy the central tenets of sound science: full disclosure of underlying data and no sponsor interference with the design of the study or release of results. As with the medical journals, EPA should disclose the sponsor of the research for all the key articles it relies upon for its decisionmak-

ing. Third, EPA must establish a peer review process that eliminates panelists with actual or potential conflicts of interest. Given the problems reported by the medical journals, it cannot rely exclusively on peer review by others, even peer-reviewed articles that have been published. Fourth, since many scientists are biased in the sense that they have strong opinions, peer-review panels must be balanced with regards to scientific view. To achieve the crucial objective of preventing the domination of peer review by one or another self-interested constituency, EPA must conduct expanded recruitment of experts who have no conflicts and represent a full range of scientific view. Fifth, EPA must reserve for its staff the sensitive task of writing toxicological profiles and should never again delegate such work to self-interested industry scientists. Last, increased government funding for basic research would go a long way toward making the first five reforms possible.

To implement the first reform, EPA scientists should make it their overriding priority to compile a research agenda based on such factors as the prevalence of a chemical in commerce and in the environment; the seriousness of its suspected adverse health or environmental effects; and the state of our ignorance of the chemical's toxicological properties. Once a list of priorities is developed, and the expense of further research can be estimated more accurately, the agency will be in the position to convince the executive branch and affected industries that further research is urgent.

Ending any consideration of studies that breach core principles of research ethics is the easiest reform to implement, and is most akin to the joint policy statement announced by the world's leading medical journals. Indeed, it is hard to imagine anyone arguing the converse of this proposition: namely, that EPA staff should rely on research findings to revise regulatory requirements even when they have never seen the underlying data that supports those conclusions. This principle is particularly important in the context of studies funded by entities with a financial stake in the regulatory decisions that the studies ostensibly inform, although it should by rights apply across the board to any piece of scientific evidence offered for EPA's consideration. It is worth noting that the government gives agencies specific powers in this regard for studies that they fund. Office of Management and Budget Circular A-110 specifies that an agency is entitled to unrestricted access to grantees' records related to the award, including research data. To accomplish this reform, EPA should require that authors of studies submitted for its consideration sign comprehensive statements regarding their funding sources and the limits imposed by their research contracts. EPA should publicize the sources of funding for each major study it relies upon for its decisions.

Suspending decisions until scientists tell us exactly what will happen makes no more sense than forcing people to self-insure or refusing to engage in long-term military planning

As for the troubled peer-review process, EPA should not recruit candidates with actual or potential conflicts of interest to serve on SAB advisory committees (including subcommittees) or any other panel of scientific experts convened to provide EPA with advice. Conflicts of interest should encompass any financial interest that would impair the individual's objectivity, including such characteristics as stock ownership or employment by an organization with a direct financial interest in the outcome of the review, such as the award of research grants. If the prohibition on nominees with conflicts of interest makes it impossible to convene a panel consisting of members with sufficient expertise to give EPA the advice it is seeking, the administrator should waive such conflicts in written, individualized determinations subject to public review. EPA may include candidates with actual or potential bias regarding the issues to be addressed by the panel, provided that the panel's overall membership is balanced. In this context, bias should encompass any predisposition resulting from professional affiliation, previous work, social relationship, or conflict of interest that could influence the

candidate's views of the information or policy alternatives at stake in the panel's deliberations.

At the moment, candidates for EPA peer-review panels and other scientific advisory functions are selected from an existing list kept by the SAB staff. The agency clearly needs to develop a larger pool of scientific experts qualified to serve on SAB committees and panels. Within legal constraints, the administrator should explore ways to compensate scientific experts at the prevailing market rate for their services, both to expand the pool of candidates and to eliminate the advantage of industry-funded scientists who are able to earn a living doing such work.

The precautionary principle lies at the heart of the controversy over the role of science in the regulatory state. The principle means taking action to prevent harm to human health or the environment, even if the relationship between the cause and the effect is not fully established scientifically. As applied, it can mean taking preventive measures to reduce pollution; shifting the burden of proving the safety of polluting activities to those who wish to engage in them; or searching for safer alternatives to releasing the pollutant into the environment. Or, as Governor Whitman put it so well: "The absence of certainty is not an excuse to do nothing."

Some commentators have argued that application of the precautionary principle is essentially a policy choice, implicitly suggesting that scientists leave the room when such decisions are made. At the opposite end of the spectrum, conservative commentators argue that when science becomes uncertain, the only alternative is to work harder to make it better, forestalling regulatory action until a reasonable level of certainty can be achieved.

While both arguments are extreme, the second is transcendent at the moment and is likely to prove far more harmful to the credibility of science over the long run. By cloaking a decision not to act as a purely scientific judgment, scientists are saddled with the burden of being wrong, of failing to take protective action in the face of what emerges as a real threat. When the sources of financial support for additional research are obviously self-interested, the public will be left with the clear impression that science was sold to the highest bidder.

We cope with uncertainty in all aspects of modern human endeavor. The whole concept of insurance is based on the proposition that we can try to predict the future on the basis of facts about the past, but in the end are willing to pay a fee to ameliorate the consequences if we end up among the injured. If we were certain what the future would bring, insurance would be unnecessary because we could either save funds to address the risk, or make plans to avoid the risk.

Only by acknowledging that it is the exceptional case where we will have definitive data can we hope to restore science to its rightful place in environmental decisionmaking

Similarly, as the United States becomes the world's dominant peacekeeper, we are constantly faced with the imperative of predicting the worst case scenarios that could occur in such situations and doing everything possible to ensure both the success and the safety of our military forces. No public official would consciously decide to absorb more casualties in order to lower the costs of equipping our troops to cope with such scenarios, although those precautionary measures often are triggered by no more than an educated guess by experts.

Like insurance underwriting or defense, environmental regulation needs to encompass the best information available at the time a decision must be made. Suspending decisions until scientists tell us exactly what will happen makes no more sense than forcing people to self-insure or refusing to engage in long-term military planning. Only by acknowledging that it is the exceptional case where we will have definitive data can we hope to restore science to its rightful place in environmental decisionmaking. •